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The Ins and Outs of Venous Access: Part II

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Long-term venous access is accomplished through the use of peripherally inserted central catheters (PICC), tunneled central venous catheters (CVC), or implantable venous access ports. (Fig. 1) Long-term access should be considered for IV therapy requiring longer than 6 to 8 weeks.

Peripherally Inserted Central Catheters

The PICC has evolved over the years. In 1945, Meyers described inserting 9- to 12-inch plastic tubing into an antecubital vein for antibiotic administration.¹ In 1957, Ross first described the use of peripherally inserted CVC to allow infusion of highly concentrated solutions based on the principle of instant dilution of infused fluids as they enter the superior vena cava.¹ In 1972, Sketch et al² compared the use of 8-inch and 21-inch polyvinyl chloride percutaneously placed peripheral catheters. They found a significantly lower incidence of thrombophlebitis with the longer catheters (4% versus 21%). The incidence of thrombophlebitis increased significantly when the shorter catheters were used to infuse antibiotics, potassium chloride, and lidocaine drip.

The PICC used today was first described in 1975 by Hoshal.³ His was the first report of the successful long-term use of PICC for administering parenteral nutrition (PN). These catheters are long (50 to 60 cm) and made of silicone. They are inserted in the antecubital fossa through the cephalic or basilic vein and threaded proximally into the distal superior vena cava. The basilic vein is the preferred site because it is the most direct route into the central veins (Fig. 2). Often catheters threaded through the cephalic vein cannot negotiate the acute angle where the cephalic vein enters the axillary vein. The 2 other structures in the antecubital fossa that should be identified and avoided are the brachial artery, which lie immediately below the medial

basilic vein and the median nerve, which lie beside the brachial artery and vein and deep to the basilic vein. Puncture of the artery can result in bleeding and hematoma, and injury to the median nerve can cause neurologic impairment.¹ These catheters are made of polyurethane or silicone.⁴ Most of these catheters are very soft and require the use of a guidewire or stiffening stylet. The 2 main techniques of insertion are through an introducer (tear-away sheath or break-away needle) or by the Seldinger technique over a guidewire.⁵⁻⁸ Venography, fluoroscopy, and ultrasound guidance have been used to assist PICC insertion. Image guidance has become the standard of care in some facilities and is especially helpful when there is poor visualization of antecubital veins.^{9,10}

The combined results of 4 studies¹¹⁻¹⁴ show that PICC were successfully inserted percutaneously in 75% (1715/2285) of the patients attempted. In 2 studies,^{12,14} PICC were successfully inserted by cut-down technique in 81% (166/205) of patients in whom percutaneous insertion was unsuccessful. In another study,¹³ a higher success rate was found with fluoroscopic insertion, 98.7% (153/155), compared with bedside insertion, 74% (111/150). The average duration of catheterization with PICC has ranged from 10 to 73 days,^{13,15-17} with some reports^{1,12,13} of PICC lasting successfully for 307 to 421 days. This proves that PICC can be used for both short-term and long-term venous access. Further studies are needed to determine how long PICC can be left in place safely and whether routine replacement is indicated.¹⁵

Indications for PICC are the need for intermediate to long-term venous access in general or the need for central venous access. PICC can be used successfully for any type of IV therapy, including central parenteral nutrition, and it can also be used for blood drawing.¹⁵ Contraindications for PICC include sclerosis, thrombosis, or thrombophlebitis of the veins in the antecubital fossa or the more proximal veins. PICC should not be inserted into the antecubital fossa in the presence of inflammation (cellulitis, dermatitis, etc), infection, burns, arterial-venous fistula, lymphedema, or ipsilateral axillary node dissection. PICC are available in various diameters. PICC are long catheters and there is substantial resistance to the infusion. Therefore PICC are not recommended for high-volume fluid infusion, rapid boluses, apheresis, or pressurized injections.⁴

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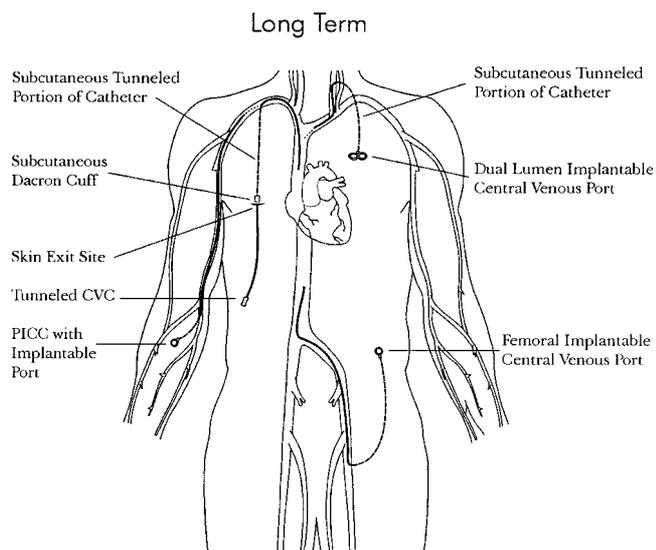


Figure 1. Drawing showing the access sites for long-term central venous access. CVC, central venous catheter; PICC, peripherally inserted central catheter.

Common complications associated with PICC include malposition, phlebitis, thrombosis, catheter occlusion, and infection (local or systemic).^{1,4,13,18} The proper placement of the tip of the PICC is the distal superior vena cava near the junction with the right atrium, as with the CVC. Malposition occurs frequently with PICC. The catheter may not be inserted far enough, and the tip may lie in the axillary vein or midportion of the subclavian vein. This can be avoided by accurately measuring external landmarks on the patient to determine the necessary length of catheter for proper placement. Most commonly PICC inserted through the basilic vein are wrongly positioned in the internal jugular vein, and those inserted through the cephalic vein are most commonly malpositioned in the axillary vein.¹⁸ A chest x-ray is mandatory after placement to confirm that the tip is positioned in the superior vena cava if central venous access is necessary.¹⁹

In some cases, prolonged venous access is required but central venous access is not necessary, such as for the administration of IV fluid therapy or IV antibiotics. In these cases, the catheter can be cut to a length equal to the distance from the insertion site to the midclavicular area so that the tip will be inserted into the midclavicular portion of the subclavian vein. The advantage of this midclavicular catheter is that x-ray confirmation of position is not required, which is convenient when inserting in the home care environment, where x-ray equipment is not readily available. Some authors recommend that radiography of midclavicular catheters be done because often (25% to 33% of the time) the catheter is malpositioned, coiling in the axillary vein or traversing into small branches or tributaries of the axillary vein. These midclavicular venous catheters should be considered extended peripheral venous catheters, and they should not be used for therapies

such as central parenteral nutrition and other toxic or sclerosing medications that require infusion into a central vein.¹ Midline catheters, midclavicular catheters, and PICC look the same on external inspection. Questions about which type of catheter has been placed in a patient should be clarified by chest x-ray to document tip placement before administering any therapy that requires central venous access.

Phlebitis rates compiled from published studies were 9.2% (112/1216), with a range of 2.2% to 26.0%.^{4,13,14,16,17,20} The incidence of catheter-related venous thrombosis with PICC has been reported to be between 0% and 7%.^{1,21} As previously discussed, 1 factor that correlates with thrombosis is position of the catheter tip. One study showed that the incidence of thrombosis was lower when the tip of the PICC was in the superior vena cava compared with in the subclavian vein (14% versus 60%, $p < .05$).¹

The incidence of PICC catheter occlusion has been reported to be from 2% to 18% and seems to be lower with therapies used on a daily basis over a prolonged period, such as PN, compared with more intermittent therapies, such as antibiotics and chemotherapy.²¹ In addition to fibrin sheaths forming around the catheter and clots forming at the tip of the catheter, blood can reflux through the tip of the catheter and form a clot inside the catheter tip. PICC should be flushed after each use and daily to prevent occlusion.¹⁰ The use of heparin flush is controversial.

A Groshong PICC has a pressure-sensitive 2-way valve at the IV tip of the catheter that prevents reflux of blood into the catheter, which should decrease the risk of occlusion by this mechanism. However, with aspiration of the catheter, the valve will open inward and blood can be aspirated through the catheter for purposes of blood drawing. Since

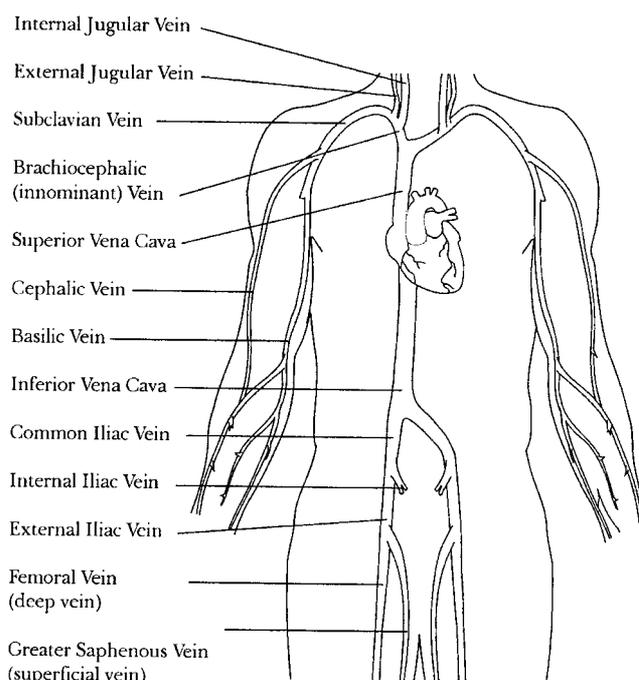


Figure 2. Venous anatomy of upper and lower extremity.

blood cannot reflux into the catheter, the Groshong catheter need only be flushed with saline, and heparin is not necessary. One study²² compared 58 Groshong PICC with 58 standard PICC and found a significantly lower incidence of clotted catheters with the Groshong PICC (2% versus 28%, $p < .001$). There was also a cost savings because heparin flushes were omitted and there was less use of thrombolytic agents for catheter occlusion. Groshong catheters will be discussed in more detail later under tunneled CVC.

Some authors contend that maximal barrier protection is not necessary during insertion of PICC because the procedure is similar to that used for short peripheral catheters. The use of maximal barrier protection has never been advocated during the insertion of short peripheral IV catheters.¹ The rate of catheter-related bloodstream infection (CR-BSI) associated with PICC is low; however, it is not insignificant, with a range of reported occurrence from 0% to 3.1%.¹ In addition, PICC usually remain in place for prolonged periods compared with the 48 to 72 hours for short peripheral catheters. As discussed in part I of this article, maximal barrier protection decreases the infectious complications associated with CVC, so the use of maximal barrier protection is also recommended for PICC insertion.²³

PICC seem to have a lower infection rate than short-term CVC, although the data are contradictory.^{15,21,24-26} The lower infection rate may be the result of factors that include colonization rates, skin moisture and temperature, and proximity to contaminated sites. Studies comparing the density of skin flora in different parts of the body have shown lower density of both aerobic and anaerobic bacteria in the forearm as compared with the head and chest. This is probably because of the increased number of sebaceous glands and subsequent higher density of lipophilic organisms in these areas. Additionally, skin temperature is lower, and there is less moisture on the clothed and bare forearm compared with the chest and neck, and bacteria prefer warm, moist environments. This also emphasizes the importance of avoiding occlusive catheter dressings and emphasizes the benefits of using dressings with a high water vapor moisture permeability to decrease the replication of bacteria under the dressing on the skin around the catheter. The PICC antecubital insertion site is away from nasal, oral, tracheostomy, and endotracheal secretions, which can more easily contaminate catheters in subclavian or internal jugular vein sites.^{1,15}

Other less common complications include perforation of the vein, extravasation, chest pain, chest wall abscess, neurologic impairment, pseudotumor cerebri, cardiac tamponade, arrhythmia, and shearing of the PICC with distal embolization.^{1,4,13} Fortunately, the latter complication is rare and is usually caused by an error in technique in which the PICC is pulled back through the insertion needle in an attempt to reposition the catheter. This should

never be done. If it does occur, the embolized portion of the catheter can usually be retrieved using a transvenous basket retriever.²¹

Ng et al¹² reported the results of 1000 consecutive PICC attempts in which there was a 96.3% rate of successful insertion, but cutdown was required in 14.6% of the patients. Complications occurred in 170 of the 963 successful insertions (17.7%). However, in 92 of these, the complication was shown as multiple attempts required for insertion. Excluding these, the complication rate was 8.1%. The most common complications in the PICC that were inserted successfully were dislodgment (8.9%), malpositioning (5.8%), phlebitis (3.8%), clotting of the catheter (3.8%), and bleeding (0.5%). Catheter infection occurred in 3.8% of the catheters, and the PICC was removed because of suspected infection in an additional 3.6%. Subsequent investigation could not confirm that the infection was caused by the PICC in these patients, however, and the confirmed infection rate was 11 infections per 10,000 catheter days.

Duerksen et al²⁵ retrospectively compared 209 PICC with 285 CVC used for PN. The mean number of days of catheter use was 10.6 for the PICC group and 12.6 for the CVC group. The PICC group had a significantly higher incidence of malposition (9.6% versus 1.8%, $p < .001$), severance or leakage (13.9% versus 1.8%, $p < .001$), and phlebitis (11.5% versus 1.8%, $p < .001$) than the CVC group. The PICC group had a lower incidence of sepsis (0.9 versus 2.2 episodes/1000 catheter days, $p = .26$) and thrombosis (0.5 versus 1.9 episodes/1000 catheter days, $p = .17$) than the CVC group, but the differences did not reach statistical significance. The main advantage of the PICC was that insertion was accomplished by specially trained nurses, whereas a physician must insert CVC.

A retrospective study by Alhimyary et al²¹ compared the use of PICC and triple lumen subclavian vein CVC for delivering PN. Most patients completed their course of PN using a single catheter without complications (84.1% for PICC group and 84.7% for the CVC group). The average number of days of PN per patient was 10.2 for the PICC group and 8.0 for the CVC group. The incidence of total complications was not significantly different between the 2 groups (16% for the PICC group versus 15% for the CVC group). The only 3 major complications (1 pneumothorax and 2 CR-BSI) were in the CVC group; however, this was not significantly different than the 0% major complication rate in the PICC group. Coiling or malposition of the PICC line was the most frequent complication in this group, occurring in 5.1% of the patients versus 4.4% of the CVC patients. All cases of catheter occlusion,²⁷ venous thrombosis,²⁶ and phlebitis⁵ occurred in the PICC group, but none of the differences was statistically significant. The authors concluded that PICC catheters can be used safely and effectively for PN and have acceptable complication rates compared with CVC.

Table 1 lists the advantages and disadvantages of

PICC in comparison to other long-term vascular access devices.

Tunneled Central Venous Catheters

The use of tunneled CVC for long-term insertion was first described by Broviac et al²⁸ in 1973, who reported the use of this catheter in 22 patients. Subsequently, this became known as a Broviac catheter. It was a 90-cm long, silicone catheter with a dacron cuff midway along the catheter. The catheter was tunneled through the subcutaneous tissues for at least 10 to 15 cm to separate the skin exit site, where the catheter came out of the skin, from the vein entrance site, where the catheter entered the vein. It was hoped that this would decrease the possibility of microbes migrating along the external surface of the CVC and causing CR-BSI. The Dacron cuff was positioned somewhere along the subcutaneous portion of the catheter and stimulated fibrosis between the cuff and the subcutaneous tissues. This anchored the catheter in place and decreased inadvertent removal of the catheter. It also provided a mechanical barrier to bacterial migration along the catheter. The catheter was inserted into the subclavian vein percutaneously in 59% of the patients. In the remainder of the patients, the catheter was inserted through a cutdown on the cephalic vein in the shoulder or the jugular veins in the neck. The tip of the catheters was positioned in the mid right atrium. Hickman et al²⁹ reported the use of a similar but slightly larger diameter catheter in 1979, which became known as a Hickman catheter.

Since the Broviac and Hickman catheters were first described, similar tunneled CVC have been manufactured under various brand names; however, many health care providers continue to refer to tunneled CVC catheters as Broviac or Hickman catheters. The most appropriate term is tunneled CVC. Routine evaluation of the veins of the upper extremity with venography or ultrasound is not performed, although evaluation may be helpful before attempting insertion in patients who have had CVC previously to rule out thrombosis or stenosis of the central veins.

These catheters are usually inserted in a surgical setting, although they have been inserted at the bedside³⁰ or in the angiography or fluoroscopy suite.^{31,32} Outpatient insertion can be safely performed.³³ Local anesthesia with IV conscious sedation is usually administered, but local anesthesia alone or general anesthesia can be used in selected patients. The majority of catheters are now inserted percutaneously through the subclavian or internal jugular vein using a Seldinger technique with a vein dilator and tear-away introducer sheath. However, cutdown on the internal jugular vein in the neck or cephalic vein in the deltopectoral groove on the anterior shoulder can be used for access to the central veins.^{30,34} Occasionally, the subclavian vein and its contributory veins may become thrombosed

or sclerosed in patients who have had long-term vascular access devices, especially if multiple sites have been accessed or if the patient has experienced multiple episodes of catheter-related infection. In these situations, the inferior vena cava can be accessed through radiologic guidance using a percutaneous translumbar approach, threading the catheter into the right atrium. This technique was first described by Kenney et al³⁵ in 1985, and several subsequent reports have shown this technique to be safe and successful in adults and pediatric patients.³⁶⁻³⁹

To avoid complications and ensure proper catheter function, the tip of the catheter should be positioned in the distal superior vena cava near the junction with the right atrium. Fluoroscopy should be used in the operating room, at the bedside, or in the fluoroscopy suite to ensure proper tip placement.^{30,31} However, if a percutaneous technique was used, a postprocedure chest x-ray should be obtained to confirm final catheter position and rule out pneumothorax. If fluoroscopy is not used and the postprocedure chest x-ray reveals that the catheter is not in the proper position, a second procedure will be necessary to reposition the catheter. Ultrasound guidance can also be used to assist in vein cannulation and subsequent tunneled CVC placement.^{40,41}

Tunneled CVC can be accessed and used immediately after insertion and confirmation of placement. The catheter needs to be flushed after each use and daily. Traditionally, tunneled CVC have been flushed with heparin 100 U/mL, although only 2 studies have been published on this topic. The first⁴² was a nonrandomized study comparing the use of 10 U/mL heparin with the use of 100 U/mL heparin. There was no difference in the incidence of thrombosis between the 2 groups. The other study⁴³ was a prospective, randomized, controlled trial of ambulatory pediatric patients with cancer who had indwelling CVC. The study compared heparin flush with normal saline flush. There was no difference in the incidence of catheter occlusion or vein thrombosis, but the normal saline group had a slightly higher rate of catheter-related infections. Controversy remains about whether to use heparin or normal saline flushes for tunneled CVC.

Removal of the catheter requires a minor surgical procedure that can be performed in the clinic, in the office, at an outpatient facility, at the bedside, or in the operating room. An incision is made over the dacron cuff and it is dissected free of the surrounding fibrosis. The catheter can then easily be removed.

Tunneled CVC and short-term CVC have the same complications. These include catheter malposition, which may occur at the time of insertion or may occur later as a result of spontaneous migration of the catheter tip to another venous location. Correct catheter tip placement is important in preventing catheter-related complications. For that reason, fluoroscopy should be used during positioning of the catheter tip, and an upright chest x-ray should be obtained after the procedure to confirm final tip

placement. Although routine periodic chest x-ray is not indicated to confirm catheter tip placement, a chest radiograph should be done if there is any sign or symptom of catheter malposition. Malpositioned catheters should be repositioned or removed and reinserted, especially if the patient is experiencing any symptoms or if the patient is receiving any hypertonic or sclerosing agents.⁴⁴

The incidence of occlusion and thrombosis increases with length of time the catheter is in place, making these complications more common with long-term CVC. Thrombosis can cause occlusion of the catheter, occlusion of the vein (deep vein thrombosis [DVT]), or both. Thrombus formation around the catheter, a fibrin sheath, is very common. In 1 study,⁴⁵ venograms were made during removal of 93 electively removed tunneled CVC. Fluoroscopy was used to view the injection of contrast medium through the catheter as it was being pulled out of the vein. Only 11% of the catheters were free of any degree of thrombosis or fibrin sleeve. A fibrin sheath was seen in 85% of the catheters and frequently dislodged when the catheter was being removed; however, no symptoms of pulmonary embolus occurred. Catheter tip obstruction and nonoccluding thrombus adherent to the wall of the vein were each seen in 2% of the patients.

In another study, complications were categorized as the first complication for that catheter or as a secondary complication.⁴⁶ The most frequently identified and the most common initial complication with tunneled CVC was inability to aspirate blood even though the catheter flushed easily. This was probably the result of a thrombus at the end of the catheter causing a ball-valve effect. Another common cause for inability to aspirate blood is positioning of the catheter tip against the vein wall such that aspiration results in the wall being sucked up against the tip, causing occlusion. In the study by Tolar and Gould,⁴⁶ catheter-related venous thrombosis occurred more commonly as a second complication, often after blood could no longer be aspirated from the catheter, indicating a cause-effect relationship. Haskal et al⁴⁷ described a technique for transvenous removal of fibrin sheaths from tunneled hemodialysis catheters. The procedure was successful in 22 of 24 catheters and restored dialysis flow rates through the catheters.

Occluded catheters can often be salvaged by administering thrombolytic therapy.⁴⁸ Initially, streptokinase was the thrombolytic agent of choice, but this was replaced by urokinase, which has a lower incidence of bleeding complications. Urokinase (Abbokinase, Abbott Laboratories, Abbott Park, IL) was manufactured from human neonatal kidney cells, so there was a risk of transmission of viral illness from the donor mother or fetus. In January 1999, Abbott discontinued production of Abbokinase because of concerns over inadequate screening for hepatitis C. It is not currently available for use.⁴⁹ However, a genetically engineered derivative, recombinant prourokinase, which has no potential for transmission of

virus, has been developed and is being tested.⁵⁰ Recombinant prourokinase has not yet been approved by the Food and Drug Administration (FDA). Recombinant tissue plasminogen activator (TPA) has also been used for occluded venous catheters. In a prospective, randomized, controlled trial, Haire et al⁵¹ showed a significantly better success rate of restoring full function to occluded CVC with TPA compared with urokinase (89% [25/28] versus 59% [13/22], $p < .05$).

DVT of the upper extremity veins was previously thought to be rare and inconsequential.^{52,53} However, it is being diagnosed with increased frequency and has been associated with CVC, hypercoagulable states, and previous lower-extremity DVT.⁵² Like lower extremity DVT, upper extremity DVT can cause chronic venous insufficiency and pulmonary embolus (PE). Additionally, acute thrombosis of the superior vena cava can cause shock and death.^{54,55} Previously, it was felt that thrombi in the upper extremity veins were more adherent to the wall of the vein and therefore had a lower propensity for PE compared with lower extremity DVT. However, more recently, studies have shown that PE occurs at least as often in upper extremity DVT.^{52,53}

Prandoni et al⁵² reported on 58 consecutive patients with signs and symptoms of upper extremity DVT. On further investigation, only 27 (47%) of the patients were confirmed to have DVT, and 30% of these patients had central venous catheters in place. Of the 27 patients with confirmed upper extremity DVT, 3 (11%) had symptomatic PE at the time of referral, and results of ventilation quantitation imaging scans were highly suggestive of PE in an additional 5 patients. Therefore, 36% of the patients with upper extremity DVT were thought to have experienced a PE. Long-term follow-up on these patients revealed a 7% incidence of recurrent upper extremity DVT; 4% died of subsequent PE, and 15% developed postthrombotic sequela. Upper extremity DVT should be considered to be the same disease as lower extremity DVT and should be treated aggressively.^{52,53}

Thrombosis of the superior vena cava has been associated with central parenteral nutrition,⁵⁴⁻⁵⁸ with the reported incidence ranging from 8% to 14%.^{55,59} Data from 1 study suggested that DVT might occur more frequently with subclavian vein CVC compared with internal jugular vein CVC.⁵⁶ Standard treatment consists of anticoagulation with heparin initially and then with coumadin.^{55,58} However, there are no clear recommendations about how long anticoagulation therapy should last. Fibrinolytic agents, including streptokinase, urokinase, and TPA, have also been successfully used for this purpose.⁵⁴⁻⁵⁸ In addition, there are no clear recommendations regarding whether the CVC should be moved to a new site or whether PN should be stopped and, if so, for how long. Some authors have suggested prophylaxis to prevent DVT. Bern et al⁶⁰ demonstrated in a randomized, prospective, controlled trial that patients who received low-dose

warfarin, 1 mg orally once a day, had a decreased incidence of catheter-related vein thrombosis compared with control patients (10% versus 38%, $p < .01$). Others have suggested periodic cleansing of the catheter prophylactically with fibrinolytic agents. This method is expensive and requires further study.⁶¹

Infection is the most common complication with long-term venous access devices, ranging from 4% to 60%.⁶² In addition to wound infections at the skin exit site, colonization of the catheter, and CR-BSI, infection can develop in the subcutaneous tunneled portion of the catheter. These are called tunnel infections. The incidence of CR-BSI with tunneled catheters is quite variable, ranging from 0.95% to 26.0%^{45,59,63,64} and probably depends on the length of patient follow-up. For this reason, the rate of CR-BSI is often reported in episodes per 1000 catheter days, with reports averaging 1.4 to 2.3 episodes of CR-BSI per 1000 tunneled catheter days. In 1 study, 9 tunneled CVC were removed because CR-BSI was suspected. CR-BSI was proven in only 3 of the cases, meaning that 6 catheters were removed unnecessarily.⁴⁵

Pathogenesis of all types of infections in all types of catheters is by one of the following four mechanisms: 1) deposition of microorganisms on the catheter at the time of insertion; 2) migration of microorganisms through the skin and along the catheter; 3) contamination of the catheter hub, tubing junctures, or infusate; and 4) seeding of the catheter from distant focus of infection. Multiple strategies have been tried to reduce the incidence of catheter-related infections with tunneled catheters. Many of these ideas have also been discussed previously in Part I of this article.²³ It is presumed that tunneling the catheter decreases the risk of colonization and CR-BSI. However, in 1 study, immunocompromised patients were randomized to receive either silicone tunneled CVC or a polyurethane nontunneled CVC.⁶⁵ The tunneled catheters had similar rates of colonization (13% [14/107] versus 11% [12/105], $p = .71$) and CR-BSI (2% [2/107] versus 5% [5/105], $p = .28$) compared with the nontunneled catheters.

Raad et al⁶⁴ retrospectively compared patients who had a silicone PICC (154 patients) with those who had a silicone nontunneled subclavian vein CVC (188 patients). The mean duration of catheter insertion was 87 days and 136 days, respectively. There was no significant difference between the 2 groups in the incidence of CR-BSI (3.9% versus 2.7%, respectively) and total catheter infections (16% versus 11%), which included CR-BSI, catheter colonization, and site infections. Because the nontunneled catheters could be inserted at the bedside rather than in the operating room, the estimated costs were much less than for Hickman-type tunneled CVC (\$582 versus \$2814 to \$3227). However, because the PICC can be inserted by a nurse rather than by a physician, it is even less expensive, approximately \$300. Ng et al¹² estimated the charges (hospital and professional fees) for insertion of tunneled CVC at

\$2602 compared with \$669 for PICC. This nontunneled silicone subclavian catheter is commercially available through several companies. One of the brand names is the Hohn catheter. This catheter has been recommended by at least 2 other authors as an alternative to tunneled catheters for intermediate to long-term access.^{66,67}

Antimicrobial impregnated cuffs^{66,67}, also have been used with tunneled CVC. One study randomized patients to receive a tunneled catheter with a silver-impregnated cuff proximal to the standard dacron cuff (108 patients) or a single dacron-cuffed tunneled catheter (92 patients).⁶⁸ The incidence of CR-BSI (32% versus 36%, respectively, $p = .61$) and tunnel infections (2% versus 0%, respectively, $p = .21$) was similar for both groups. Hemmerlein et al⁶⁹ found in an *in vitro* study that the silver-impregnated cuffs are cytotoxic to human fibroblasts. This may decrease the ability of the cuffs to anchor to subcutaneous tissues and may increase the incidence of inadvertent catheter removal. The results of studies on the use of prophylactic systemic antibiotics to decrease the incidence of catheter-related infections have been contradictory.⁷⁰⁻⁷³

Another prophylactic measure is the antibiotic lock, in which a high concentration of antibiotic (vancomycin, amikacin, or minocycline) is added to the heparin flush solution used to flush the catheter when not in use.⁶² One study randomized 45 children with oncologic or hematologic disorders who had tunneled CVC to receive flushing with either plain heparinized saline (24 patients) or a solution of heparinized saline and vancomycin (21 patients).⁷³ The vancomycin group had a significantly lower incidence of CR-BSI (0% versus 21%, $p < .05$). However, antibiotic locks could increase the risk of infection with antibiotic-resistant microbes, and more studies are needed in this area.^{15,62}

Skin exit site infection is treated with warm, moist compresses. The frequency of site care should be increased, and in selected cases, oral or parenteral antibiotics should be administered.^{62,75} Tunnel infections usually require removal of the catheter; although sometimes the catheter can be saved by administering a prolonged course of IV antibiotics.^{62,75} The standard treatment for CR-BSI is removal of the catheter. However, if the patient requires ongoing long-term venous access, and the infection is not secondary to fungus or polymicrobial infection, a trial of 4 to 6 weeks of parenteral antibiotics can be tried. If the patient has persistently positive blood cultures after 48 hours of antibiotics, or if the patient has recurrent sepsis following antibiotic therapy, the catheter must be removed.^{62,75} The reported success rate of antibiotic treatment ranges from 30% to 91%.^{75,76} In 1 study of patients receiving home PN, a select group of patient with CR-BSI was treated with 4 weeks of systemic antibiotics. Treatment was successful, and the catheter was saved in 87% of patients with Gram-positive infections and in 53% of patients with Gram-negative infections.⁷⁷

Another proposed treatment for CR-BSI is the use of intraluminal antibiotics instilled in the catheter each day for 2 weeks and allowed to remain for 8 to 12 hours. The antimicrobial agents used are gentamicin, vancomycin, or amphoteric B. The choice of agent depends on whether the infection is Gram-negative, Gram-positive, or fungal in origin. Benoit et al⁷⁶ used this treatment in 9 episodes of CR-BSI that occurred in 5 patients. However, peripheral blood cultures were negative in 5 of these episodes, raising the question of whether these were cases of colonization rather than of true CR-BSI. Systemic antibiotics were also used in 6 of these 9 episodes. The infection was cleared in 3 of the patients. One patient had 2 CR-BSI, and 1 patient had 3 CR-BSI, but the repeat episodes were caused by different organisms, and all of the infections were finally cleared. Further studies with larger number of patients are needed to determine the usefulness of this therapy.

Air embolism during insertion of tunneled CVC has been reported in 3 pediatric patients who received local anesthesia with IV conscious sedation.⁷⁸ The advantage of general anesthesia is that the use of positive pressure ventilation makes it less likely that air will be sucked in through the open needle or catheter. However, if the catheter or needle is open to air, and the patient is awake and takes a deep breath, such as when crying, large amounts of air can rapidly be sucked into the venous system. Other rare complications include perforation of the vein or heart with extravasation of infusate, bleeding, or pericardial tamponade.⁴⁴

Another rare complication is the pinch-off syndrome and catheter fracture. The pinch-off sign was first reported by Aitken and Minton⁷⁹ in 1984 and consists of a narrowing of the catheter as it passes between the first rib and clavicle, as seen on chest x-ray. A chest x-ray taken with the patient's arms at the side and shoulders in neutral position, not in a forward position as done with a standard chest x-ray, will best demonstrate this finding. This occurs when the catheter is being compressed between the first rib and the clavicle, causing intermittent compression and pinching, leading to intermittent occlusion of infusion and aspiration. Changes in the patient's position can widen or narrow the angle between the rib and clavicle, usually by raising or lowering the arm, which can relieve the occlusion of the catheter. This is the hallmark sign of this syndrome. The external portion of the catheter may frequently tear, requiring repair as a result of the increased pressure required to overcome the compressed catheter. The treatment is removal of the catheter and reinsertion in a more lateral position in the subclavian vein or placement in the internal jugular vein.

If this syndrome is not diagnosed and treated, the catheter can fracture, either partially or completely, at the site of compression as a result of the repeated trauma of intermittent compression between the rib and clavicle. The mean time from insertion to frac-

ture is 6.5 months, with a range of 3 weeks to 13 months. Fracture of the catheter can cause pain, tenderness, and signs of inflammation around the clavicle from infusion of the IV fluids or medications into the subcutaneous tissues. If completely transected, the distal end of the catheter can embolize into the right ventricle or pulmonary artery, requiring surgical or angiographic retrieval. Cardiac arrhythmias and even deaths from catheter embolization have been reported.^{44,80}

In the late 1980s, the Groshong tunneled CVC was designed and had a pressure-sensitive 2-way valve that prevented blood from refluxing back inside the tip of the catheter.^{30,81} Therefore, the catheter can be flushed with normal saline alone and heparinized saline flushes are not required. If the catheter is not being used daily, it only needs to be flushed once a week. Standard tunneled CVC must be flushed daily. Therefore, the maintenance cost was less with the Groshong catheter and there was less manipulation of the catheter, theoretically decreasing the incidence of breakage, thrombosis, and infections.⁸² Studies of Groshong catheter use reported good results.^{30,46,81,83} Six studies have compared the use of Groshong catheters with the use of Hickman catheters. In 4 of these studies, 1 randomized⁸⁴ and 3 nonrandomized,⁸⁵⁻⁸⁷ no significant difference was found between the 2 catheters with regard to incidence of mechanical complications,⁸⁶ thrombosis,^{84,87} or catheter-related infections.⁸⁴⁻⁸⁷ However, 2 prospective, randomized, controlled trials revealed that Hickman catheters had a lower incidence of catheter occlusion compared with the Groshong catheter.^{82,88}

Warner et al⁸² randomized 10 patients to receive Hickman catheters and 10 patients to receive Groshong catheters. The total catheter days were similar for both groups; however, the Groshong catheters required almost 3 times the number of urokinase treatments for occlusion compared with the Hickman catheters (34 *versus* 13). In addition, 2 Groshong catheters required conversion to daily flushes of heparin to maintain patency. Another 5 catheters had to be removed prematurely for the following reasons: superior vena cava thrombosis⁸⁹; frequent occlusions requiring repeated urokinase treatment²⁷; tear in the catheter just above the valve, causing leakage and chest pain when infusing through the catheter⁸⁹; and air bubbles in 1 of the lumens, causing concern for possible air embolism.⁸⁹ After removal, the latter catheter was found to have an abnormal communication between the 2 lumens. This study was terminated prematurely because of the higher complication rate associated with the Groshong catheters.

Pasquale et al⁸⁸ randomized patients to receive Groshong (55 patients) or Hickman (53 patients) tunneled CVC. There was no significant difference between the 2 groups with regard to catheter-related infections (13% *versus* 11%), catheter fracture (0% *versus* 4%), or thrombus formation (15% *versus* 15%). However, the Groshong catheters had a sig-

Table 1
Comparison of advantages and disadvantages of various long-term venous access devices (VAD)

	Advantages	Disadvantages
Peripherally inserted central catheter (PICC)	<ul style="list-style-type: none"> No risk of pneumothorax or puncture of internal carotid or subclavian arteries Can be inserted at the bedside Can be inserted by specially trained nurses Easy to remove by nursing personnel Available in single, double, and triple lumens Once inserted, does not require repeated skin puncture External portion can be repaired if torn or damaged Insertion is less costly than tunneled CVC or implantable port 	<ul style="list-style-type: none"> Restricts activities of the arm in which it is inserted More difficult to cover up so more affect on body image Difficult to perform self care because can only use one hand Requires daily maintenance and flushing Smaller and longer catheter so more prone to occlusion and may be more difficult to draw blood Usually not sutured and location on the arm increases the risk of dislodgement Must use occlusive dressing at all times Patient may not have adequate veins and insertion is unsuccessful in up to 25% of the attempts Higher rate of coiling and malposition of catheter
Tunneled central venous catheter (CVC)	<ul style="list-style-type: none"> Insertion success rate much greater than for PICC Dacron cuff in tunneled portion of catheter anchors catheter in place to decrease risk of dislodgment and decrease risk of bacteria migration along the catheter Once inserted, does not require repeated skin puncture Available in single, double, and triple lumens External portion of the catheter can be repaired if torn or occluded Can be removed relatively easily with a bedside procedure under local anesthesia Can be used for central venous pressure monitoring Single, double, and triple lumens available Catheter easily hidden under a shirt so is less obvious than PICC Insertion less costly than implantable port 	<ul style="list-style-type: none"> Requires a physician for insertion and removal Insertion requires operating room time Requires daily maintenance and flushing required Body image not as good as implantable port when port not accessed May have a higher catheter related infection rate compared to PICC and implantable port Insertion is more costly than PICC (although the incidence and cost of treating occlusion, malposition, and dislodgement may be less for tunneled CVC)
Implantable central venous port	<ul style="list-style-type: none"> Available in single and double lumens When not in use, the entire device is under the skin with no exposed tubing so body image is least effective of all the long-term VAD When not in use, requires flushing only once a month with no other maintenance Minimal interference with activities 	<ul style="list-style-type: none"> Requires a physician for insertion and removal Insertion and removal requires operating room time Requires repeated skin puncture with special needle to access the port (if being used daily, the needle can be left in and changed weekly) Not available in triple lumen Interferes with MRI and CT scans and may interfere with radiation therapy Insertion costs are the greatest of all of the long-term VAD

MRI, magnetic resonance imaging; CT, computed tomography, VAD, venous access device.

nificantly higher incidence of catheters in which intermittently blood could not be aspirated (29% versus 9%, $p < .05$) and in which blood could not be aspirated (15% versus 2%, $p < .05$). Therefore, the authors preferred the standard Hickman catheter. One prospective, nonrandomized study⁹⁰ compared flushing Groshong catheters weekly with normal saline versus heparin and found that the heparin flush decreased the incidence of intraluminal clots and improved catheter function.

The use of tunneled CVC is indicated when long-term venous access (more than 6 to 8 weeks) is required. Tunneled CVC can be used for any type of

IV therapy and for blood drawing. The advantages and disadvantages of tunneled CVC and comparisons with other methods of long-term venous access are shown in Table 1.

Implantable Central Venous Ports

Implantable central venous ports were first described in 1982.^{4,91} As with tunneled CVC, implantable central venous ports have been referred to by various brand names such as Port-A-Cath and Medi-Ports, but use of the generic term implantable central venous port is most accurate. Insertion is

usually performed in the operating room, although these catheters can be safely inserted in the angiography or fluoroscopy suite,^{31,32} and ultrasound or venography can be used to assist in vein localization.^{91,92} The patient is usually given local anesthesia with IV conscious sedation; although general anesthesia may be required in selected patients. Outpatient insertion can also be done safely.³³

Ports are available in steel, titanium, or plastic with a self-sealing silicone rubber septum on top through which the port is accessed. An incision is made in the upper chest and sharp and blunt dissection is used to form a subcutaneous pocket. The incision should be positioned to 1 side of the pocket so that once the incision is closed, the surgical scar does not lie immediately over the top of the port. This would require the access needle to pass through the scar tissue to reach the port, which would be more difficult for the person inserting the needle and more uncomfortable for the patient. Also, it is important to place the port over a firm surface of the body to ensure stability of the port when the access needle is being inserted and while the needle is in place.

A silicone catheter is then inserted into 1 of the central veins and properly positioned, as previously described for tunneled CVC. The subclavian vein or internal jugular vein is the most common veins used, although the femoral vein and even percutaneous cannulization of the inferior vena cava have been used if the upper extremity veins are not usable. The proximal end of the catheter is tunneled from the vein entrance site to the subcutaneous pocket incision, cut to the proper length, and then attached to the port. The port is accessed and aspirated to ensure good blood return and to remove any air in the system. The port and catheter are then flushed with heparinized saline. The port is inserted into the subcutaneous pocket and sutured to the underlying tissues to prevent the port from flipping over with manipulation (Figs. 1 and 3A). Fluoroscopic guidance should be used during the procedure to ensure proper tip placement, and a postprocedure chest x-ray is mandatory to document final tip placement and to rule out pneumothorax if a percutaneous method was used.

The port should never be accessed with a standard IV needle unless emergency venous access is required because these needles can core out a piece of the septum. If the septum cannot seal itself when the needle is removed, fluid and blood can leak out of the port and into the subcutaneous tissues, causing pain, infection, or thrombosis of the port and catheter. Ports should only be accessed with a Huber needle, which is tapered at the end and has the opening on the side of the needle rather than at the end of the needle like a coring needle (Fig. 3B). The Huber needle maintains the integrity of the septum, which can withstand at least 1500 to 2000 punctures. The most common Huber needles used to access ports are 19-gauge to 21-gauge. These needles come in various lengths to accommodate thick and thin subcutaneous tissues. For continuous infusions, Huber needles with a right-angle bend in the

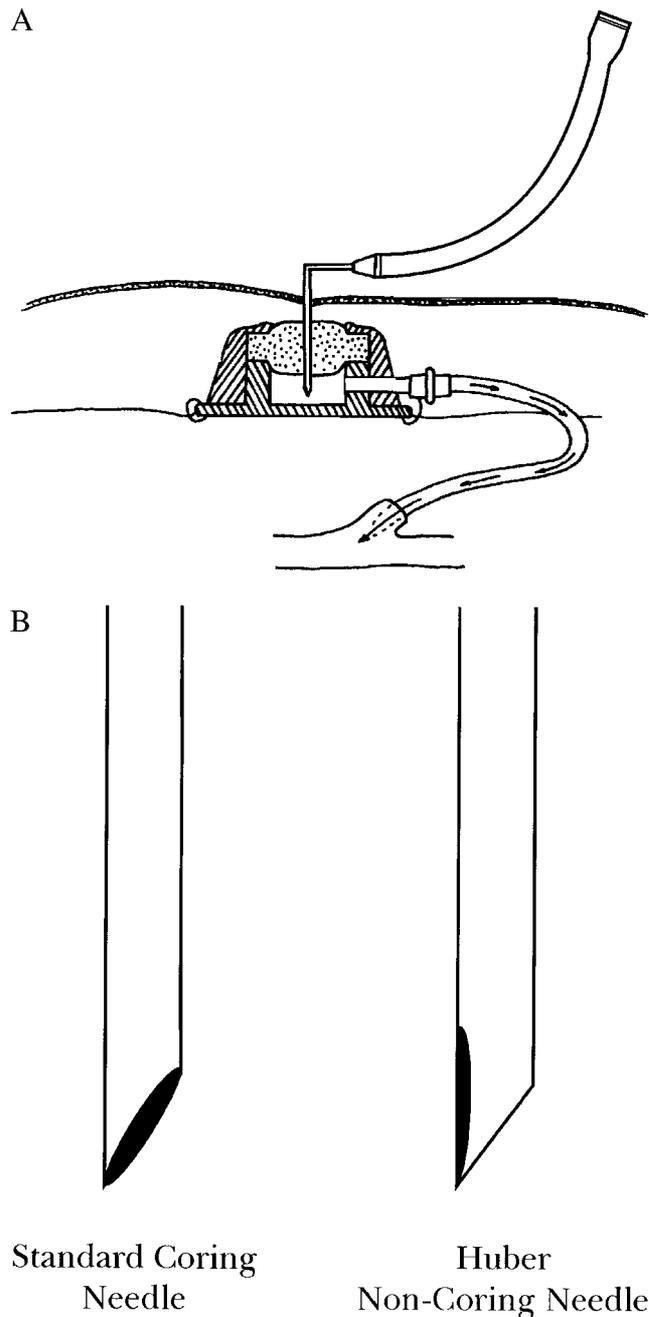


Figure 3. (A) Drawing of implantable venous port with access needle and tubing in place. (Adapted from Kupensky DT from *Journal of Intravenous Nursing* 18:198–201, 1995.¹⁰³ Reprinted with permission Lippincott, Williams, & Wilkins) (B) Comparison of the standard coring needle with the opening at the end of the needle and the noncoring Huber needle with the opening at the side of the needle.

middle are available so that the needle will rest gently against the skin. The right-angle Huber needle also has tubing attached to it that can be connected to IV tubing (Fig. 3A).^{91,94}

If venous access will be needed soon after surgery, the port can be accessed percutaneously with the Huber needle during surgery when the area is still

anesthetized.⁹⁵ The Huber needle and access line are flushed with heparinized saline, left in place, and can be used postoperatively as soon as x-ray confirmation of proper placement is obtained. This procedure eliminates the necessity of inserting the Huber needle through freshly operated, tender skin and subcutaneous tissues and alleviates the consequent pain and discomfort to the patient. Once the wound heals, there is minimal pain when accessing the port with the Huber needle. The port is accessed by palpating through the skin and feeling for the bulging septum in the middle of the port. After prepping the area, the access needle is then inserted through the skin, through the septum, and into the port in a sterile fashion.

If the port is being used daily, the Huber needle can stay in place, but it needs to be changed at least weekly. Some patients prefer to remove the needle after each day's treatment and reaccess the port daily. However, this may decrease the lifespan of the port from frequent punctures of the septum. If the port does not need to be accessed daily, the needle can be removed between treatments so that there is nothing protruding outside of the body. Usually the port is barely visible through the skin unless the subcutaneous pocket is not deep enough or the patient has minimal subcutaneous tissue. The port needs to be flushed with heparinized saline at least once a month.

A Groshong catheter, a valve-tipped catheter described in the previous section, can also be used in conjunction with an implantable port. Biffi et al⁹⁶ reported good results in a series of patients with 178 Groshong implantable central venous ports. However, no studies have compared standard silicone catheters with Groshong catheters in conjunction with implantable ports. Another modification is the peripheral implanted venous port. This is a PICC that is attached to a port implanted in the subcutaneous tissues of the forearm. The first such device was released for general use in 1989 and was called the Port-A-Cath P.A.S. Port (Pharmacia Deltec, Inc, St. Paul, MN).⁹⁷ This port is smaller than the standard chest port, and the system incorporates an electromagnetic method of catheter tip location tracking for proper positioning. This is called the Cath-Finder, and it may obviate the need for fluoroscopy during insertion. Studies using this system have shown good results; however, these are relatively small studies with no control groups.⁹⁷⁻¹⁰¹

The potential complications of implantable venous ports are similar to those of tunneled CVC.^{95,96,102} Malposition of the catheter can occur, as discussed in the previous section. Nelson et al¹⁰² reported that fluoroscopy during insertion revealed that the guidewire did not pass into the superior vena cava as intended in 9 of 70 cases (13%). In 6 of these cases, the guidewire passed into the internal jugular vein, and in the remaining 3 cases, the guidewire passed into the contralateral subclavian vein. However, fluoroscopic manipulation successfully positioned the guidewire in the superior vena

cava in all of these cases. This highlights the importance of using fluoroscopy during insertion. Malposition of the catheter would require repeat surgery to correct it. Even with fluoroscopy, the catheter position can change postoperatively when the patient sits up. This has been reported in 2% to 18% of cases.¹⁰² Therefore, an upright postprocedure chest x-ray is still mandatory to confirm the final catheter tip position. If the catheter was inserted percutaneously, the postprocedure chest x-ray is necessary to rule out pneumothorax. Postoperative malposition of the catheter is most common in obese patients and in large-breasted women.^{95,102} In these patients, the port should be placed only a few centimeters below the clavicle.¹⁰²

Catheter occlusion, as previously discussed, is a common problem with long-term venous access devices. Ryder¹ reviewed 6 studies of thrombosis associated with tunneled catheters or implantable ports. Clinical symptoms of thrombosis occurred in only 0% to 4% of patients with CVC; however, venograms on asymptomatic patients with CVC revealed thrombosis in 33% to 46% of patients. Catheter occlusion can be partial, allowing infusion of fluid but not withdrawal of blood; or it can be complete, allowing neither infusion of fluid nor withdrawal of blood. Partial occlusion can be caused by the position of the tip of the catheter against the wall of the vein, by the fibrin sheath around the catheter, or by a blood clot at the tip of the catheter. Complete occlusion can be from thrombosis of the catheter or from precipitation of medications or solutions infused through the catheter.⁶²

Kupensky¹⁰³ presented a useful algorithm to assess the cause of catheter occlusion and the optimal treatment to reopen the catheter. Occlusion of the catheter secondary to fibrin sheath or thrombosis can frequently be resolved by administering fibrinolytic agents, as previously discussed. Whigham et al¹⁰⁴ prospectively reviewed a series of 393 consecutive PICC with implantable ports placed in the forearm. Catheter occlusion occurred once in 22.9% of the patients and twice in an additional 9.2% of the patients. Urokinase was used in 76 patients at the time of their initial occlusive event, with a 98.7% success rate. However, as previously discussed, TPA is presently the most often used fibrinolytic agent. Precipitation of medications, calcium phosphate, or lipids may be cleared with infusion of bicarbonate, hydrochloric acid, or ethanol solutions, respectively. As discussed in the section on tunneled CVC, some authors have proposed prophylactic treatments to prevent catheter-related DVT. In addition to warfarin⁶⁰ and fibrinolytic agents,⁶⁰ Monreal et al¹⁰⁵ showed that daily injections of subcutaneous low-molecular-weight heparin decreased the incidence of DVT related to implantable ports (6% versus 62%, $p < .01$).

As mentioned in the previous section, infection is the most common problem with long-term CVC, including implantable venous ports. In addition to colonization of the catheter, tunnel infections, and

CR-BSI, implantable venous ports are subject to infections in the subcutaneous pocket at the site of the port, called pocket infections.⁷⁵ Pocket infections usually require removal of the catheter; although occasionally they can be successfully treated with a prolonged course of antibiotics.^{62,75} The standard treatment for CR-BSI is removal of the catheter. However, if the patient requires ongoing long-term venous access and the infection is not secondary to fungus or polymicrobial infection, a trial of 4 to 6 weeks of parenteral antibiotics can be tried. If the patient has persistent positive blood cultures after 48 hours of antibiotics, or if the patient has recurrent sepsis following antibiotic therapy, the catheter and port must be removed.^{62,75} The incidence of catheter-related infections seems to be increased in patients with HIV or acquired immunodeficiency syndrome, ranging from 0.85 to 8.7 times that of immunocompetent control patients.³⁴ However, the incidence is still fairly low and ranges from 1.2 to 2.0 episodes per 1000 catheter days.³⁴ Long-term venous access devices should therefore be used in patients with HIV or acquired immunodeficiency syndrome when medically indicated.³⁴

Implantable ports have an incidence of pinch-off syndrome and catheter fracture similar to that of tunneled CVC.^{44,106} Another cause of catheter embolization specific to implantable venous ports is separation of the catheter from the port, which is caused by slippage of the locking device.⁴⁴

The complication rates for implantable venous ports have been compared with those of tunneled CVC in 5 retrospective studies^{34,59,85,107,108} and in 6 prospective, nonrandomized studies.^{109–114} Shaw et al¹⁰⁸ demonstrated that ports had a lower total complication rate compared with tunneled CVC (46% [18/39] versus 66% [40/61], $p = .056$), although the difference did not quite reach statistical significance. One study¹⁰⁷ revealed a lower incidence of catheter occlusion with ports (0% [0/25]) versus 16% [7/45], $p < .05$, and another study¹¹⁰ revealed a slightly higher incidence of complications with ports (7% [2/29] versus 1% [1/71], $p = .20$). However, 2 studies^{59,111} compared rates of venous thrombosis and found similar rates for both devices (combined results: 6% [8/142] for ports versus 9% [24/280] for tunneled CVC, $p = .28$).

Catheter-related infections were analyzed in 8 studies,^{34,107,109–114} and all but 1³⁴ showed a lower rate of infection with implantable venous ports compared with tunneled CVC. In 2 of these studies, the difference was not statistically significant because of the small sample size. The results of 6 of these studies could be combined, and the combined results showed a significantly lower rate of total infections with implantable ports (9% [86/954] versus 35% [406/1163], $p < .001$).

CR-BSI was reported in 5 studies,^{58,85,107,108,110} and in all but 1 study,⁸⁵ the incidence was significantly lower in the port group. The combined results of these 5 studies showed a significantly lower incidence of CR-BSI with implantable ports (5%

[41/899] versus 29% [341/1172], $p < .001$). Two studies^{107,110} showed that ports had a lower incidence of local or site infections, although the difference did not reach statistical significance in 1 study¹⁰⁷ because of small sample size. However, 2 other studies^{85,108} showed that the type of device did not affect the rate of local infection. The combined results of these 4 studies showed a significantly lower incidence of site infection with implantable ports (5% [36/786] versus 9% [86/963], $p < .001$). Only 1 study¹¹⁰ specifically reported tunnel or pocket infections, and the results showed no difference between implantable venous ports and tunneled CVC (1.9% [13/680] versus 2.2% [17/788], respectively, $p = .74$).

All of these studies were retrospective or nonrandomized and therefore the results may be biased. In general, implantable venous ports are more often used for intermittent therapies such as chemotherapy, blood drawing, or blood transfusions compared with tunneled CVC, which are more often used for daily therapies such as antibiotics and parenteral nutrition. Therefore, the tunneled CVC would be accessed more often, which could account for the increased risk of infection seen in some studies. Mueller et al¹¹⁵ published the only prospective, randomized, controlled trial comparing ports and tunneled CVC. They found no differences in the infectious, mechanical, or thrombotic complications between the 2 groups.

Graham et al²⁶ retrospectively compared PICC to a variety of centrally placed catheters, tunneled silicone CVC, implantable ports, Hohn catheters, and standard nontunneled polyurethane CVC. CR-BSI occurred in 0% (0/76) of the patients with PICC compared with 4.7% (6/127) of the patients with centrally inserted catheters; however, this difference did not reach statistical significance ($p = .09$).

Smith et al²⁴ retrospectively compared long-term CVC, tunneled catheter (136 patients), or implantable ports (147 patients) with PICC (555 patients). The majority of these catheters (56%) were used for PN, and the remainder were used for antibiotic therapy, chemotherapy, and other indications. CVC had a lower rate of total complications compared with PICC (19% versus 35%, $p < .001$). CVC had a significantly lower risk of phlebitis (0% versus 6.5%, $p < .001$) and catheter malfunction (3.9% versus 11.7%, $p < .001$). The incidence of thrombosis (0.7% versus 2.5%) was also lower for CVC, although the difference did not reach statistical significance ($p = .14$). PICC had a slightly lower rate of catheter-related infections (7.2% versus 9.5%), but the difference did not reach statistical significance ($p = .24$). CVC had a higher rate of pneumothorax (1.4% versus 0%, $p < .05$); however, only 2 of the 4 CVC pneumothorax patients required a chest tube and both had no further complications. The average duration of insertion was 23 days for PICC, 125 days for tunneled CVC, and 221 days for implantable ports. Therapy was successfully completed at the time of catheter removal in 85% of patients with

CVC compared with only 76% of patients with PICC. The total insertion costs, including professional fees, was approximately \$500 for PICC, \$2500 for tunneled CVC, and \$3500 for implantable ports. However, the cost of complications must also be included, and mechanical problems were frequent with PICC. The 50 occluded PICC required at least 1 dose of urokinase, which costs \$160 per dose, and 20% of the occluded PICC could not be reopened. The occluded catheters that could not be reopened, many of the 14 damaged PICC, and 37 PICC with other complications had to be replaced, at an additional cost of \$500. Signs and symptoms of thrombosis and phlebitis were common, requiring noninvasive venous studies at a cost of \$350 per patient. Finally, 5% of PICC could not be successfully inserted at the bedside and required fluoroscopic guidance for proper position, at a cost of approximately \$1600 per procedure. Therefore, the overall cost difference between PICC and long-term CVC was not as great as the difference in insertion costs would indicate.

The implantable central venous port can be used for blood drawing or for administration of any IV therapy, including parenteral nutrition, antibiotics, and chemotherapy. Usually, if the patient requires long-term daily therapy such as parenteral nutrition, a tunneled CVC is preferred. The advantages and disadvantages of implantable venous ports and comparisons with other long-term venous access devices (VAD) are shown in Table 1.

Summary

The ideal VAD depends on what is the best choice for the best outcome at the least cost. This depends on the duration of access needed and the requirements of the treatments to be administered through the device. Long-term VAD include PICC (with external catheter or implantable port), tunneled CVC, or implantable central venous port. If the duration of access is fairly short, weeks to months, and the patient has adequate antecubital veins, the PICC catheter is probably the best choice. If the anticipated duration is months to years, then a tunneled CVC or implantable central venous port is probably a better choice. If the therapy requires long-term daily access, such as for home PN, most patients would prefer the tunneled CVC so that repeated sticks with the access needle are not required. However, some of these patients prefer an implantable port. If the therapy requires only periodic venous access, such as blood drawing, chemotherapy, or intermittent courses of antibiotics, then the implantable port is probably the preferred venous access device because it requires less maintenance and is more cosmetic.

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The Ins and Outs of Venous Access: Part I

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ABSTRACT: Selection of the proper venous access device is important to maximize patient benefit and minimize patient discomfort, morbidity, mortality, and cost. The decision of which device to use is based on whether or not the patient requires central venous access and whether the need is short-term (<6 to 8 weeks) or long-term. Short-term venous access devices include short peripheral IV catheters, midline catheters, peripherally inserted central catheters (PICC), and central venous catheters (CVC). This article reviews each of these short-term devices and their indications, contraindications, advantages, and disadvantages. Part 1 covers Venous Anatomy and Short-Term Venous Access; Part 2, to be published in the June issue, covers Long-Term Venous Access.

More than 150 million vascular access devices (VAD) are purchased annually in the United States, at a cost of approximately \$840 million.¹ Of these, 5 million are central venous catheters (CVC) or pulmonary artery catheters.¹ Approximately 500,000 long-term CVC are inserted in the United States annually, mainly for chemotherapy and parenteral nutrition (PN).¹ Although there is no absolute cutoff, long-term CVC are indicated when venous access is required for more than 6 to 8 weeks.² Before discussing the options for short-term VAD, the venous anatomy will be briefly reviewed.

Venous Anatomy

The veins of the upper and lower extremities are used for venous access; however, the upper extremity veins are usually preferred (Fig. 1). The lower extremity veins are comprised of the deep and superficial systems. The main vein in the superficial system is the greater saphenous vein, which runs

along the medial aspect of the leg, emptying into the common femoral vein just below the groin crease. The deep venous system branches also eventually empty into the common femoral vein. The common femoral vein becomes the external iliac vein after it crosses under the inguinal ligament in the groin. The external iliac and internal iliac veins join to form the common iliac veins. The right and left common iliac veins join to form the inferior vena cava, which then terminates in the right atrium.

The 2 main veins in the arm are the basilic and cephalic veins, which are situated on the medial and lateral aspects of the arm, respectively.³ In the antecubital fossa, both of these veins are superficial and are accessible for venous access; however, below and above this level, these are deep veins. The basilic vein becomes the axillary vein at the lateral edge of the chest. As the cephalic vein crosses the shoulder area, it courses through the deltopectoral groove and empties into the axillary vein in the infraclavicular area. When the axillary vein crosses over the lateral edge of the first rib, it becomes the subclavian vein (SCV). The SCV and the internal jugular vein (IJV), which drains the blood from the head and courses behind the sternocleidomastoid muscle, join to form the innominate or brachiocephalic vein. The right and left innominate veins join to form the superior vena cava, which empties into the right atrium. The external jugular vein drains the blood from the face and scalp and runs along the lateral portion of the neck in the subcutaneous tissues. It courses over the sternocleidomastoid muscle and then empties into the SCV at the base of the neck in the supraclavicular fossa. Only the inferior and superior vena cava should be considered central veins; all other veins should be considered peripheral veins.^{4,5}

Short-Term Venous Access

Devices used for short-term venous access include short peripheral catheters, midline catheters, CVC, and peripherally inserted central catheters (PICC) (Fig. 2). Short-term access can be used for anywhere from 3 days up to 6 to 8 weeks; however, if access is required for a longer period of time, long-term access devices should be considered.

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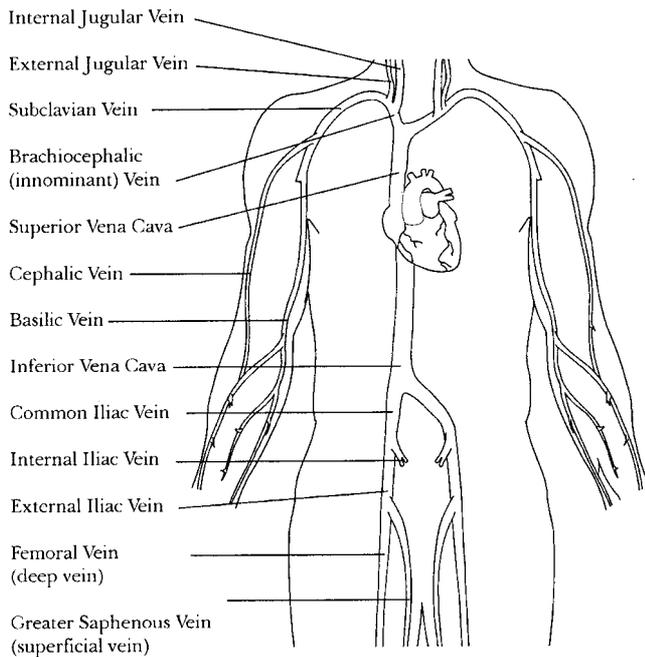


Figure 1. Venous anatomy of upper and lower extremity.

Short Peripheral IV Catheters

Short peripheral IV catheters ($1\frac{1}{2}$ inch) are inserted into the superficial veins of the hands, forearms, or antecubital fossa (Fig. 2) and are the quickest, simplest, least expensive, and most common method of venous access in general.⁶ The insertion technique is that of a catheter over the needle; that is, the device is inserted into the vein and then the catheter is advanced off of the needle and into the vein. However, the peripheral veins are prone to phlebitis and subcutaneous perivenous infiltration, and the catheter should not stay in 1 site for longer than 48 to 72 hours.^{6,7} The majority of short peripheral venous catheters in the United States are made of teflon or polyurethane. Catheters made of these materials have fewer infectious complications compared with catheters made of polyvinyl chloride or polyethylene.⁶ Steel needles were used at one time for vein cannulation in patients at increased risk of infection, but the newer teflon and polyurethane catheters have equally low infection rates and fewer risks of infiltration than the steel needles.⁶

A short peripheral catheter is indicated for peripheral PN in a patient with adequate peripheral veins. These catheters are contraindicated for patients with inadequate peripheral veins, for therapy longer than approximately 5 days, for patients with increased nutritional requirements, or for patients with intolerance to fluid load. Peripheral veins can tolerate only up to a certain concentration of solution, as will be discussed later in this section. The administration of peripheral PN requires a relatively large fluid volume to administer significant amounts of protein and calories. Patients who require more-than-maintenance amounts of protein

or calories, or who have fluid overload, pulmonary edema, or congestive heart failure may not tolerate the amount of fluid required to meet protein and calorie goals.

Potential complications of short peripheral catheters include thrombophlebitis, cellulitis, suppurative thrombophlebitis, and sepsis. Thrombophlebitis refers to the development of inflammation, subsequent venous thrombosis, and possible occlusion, which causes changes over the skin of the cannulated vessel, including erythema, edema, venous cords, and pain. The cause of thrombophlebitis is multifactorial and includes catheter material, cannula size, duration of therapy, bacterial colonization, composition of the solution, location of catheter site, blood flow, particulate matter, and infusion rate.⁴ Within a few hours of insertion of a peripheral venous catheter, sloughing and disruption of the endothelium occur, resulting in adherence of fibrin patches, polymorphonuclear leukocytes, platelets, and erythrocytes to the subendothelium. Leukocytes then progressively infiltrate through the wall of the vein to the adventitia, and thrombus develops. Another early response to catheter insertion is venous constriction, in which blood flow is decreased and irritation caused by the infusate and catheter is increased. Interactions between the catheter surface and the blood result in platelet aggregation and fibrin sheath formation around the catheter, further reducing blood flow. The pericatheter thrombus extends from the tip of the catheter proximally to the insertion site, which explains the observation of leakage of infusate from the catheter insertion site.⁴

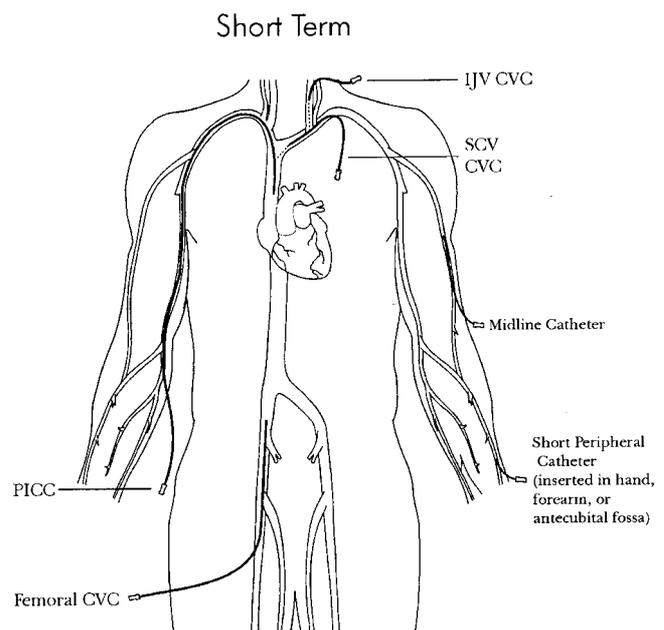


Figure 2. Drawing showing the access sites for short-term central venous access. IJV, internal jugular vein; CVC, central venous catheter; SCV, subclavian vein; PICC, peripherally inserted central catheter.

The type of solutions infused also affects the formation of thrombophlebitis. Increased osmolality and high or low pH (acidic or alkaline) of infusate solutions increase the incidence and the onset of thrombophlebitis. In addition, certain antibiotics and other medications such as vancomycin, nafcillin, erythromycin, and morphine are inherently irritating to the veins because of their chemical structure or pH despite relatively normal osmolality. Most crystalloid solutions, especially those containing dextrose, are acidic, with pH as low as 3 to 5, which is irritating to the veins.⁴ Gazitua et al⁸ studied peripheral infusion of IV fluids, primarily amino acid solutions, and found that thrombophlebitis occurred earlier and more frequently with amino acid-containing solutions compared with non-amino acid solutions. They found that the lowest risk of phlebitis occurred with solution osmolality under 450 mOsmol/L; moderate risk occurred with solution osmolality of 450 to 600 mOsmol/L; and the highest risk of phlebitis occurred with solution osmolality more than 600 mOsmol/L, which resulted in 100% phlebitis rate. Therefore, solutions formulated for peripheral PN (PPN) should not exceed 3% amino acids or 10% dextrose.⁷ Even with these concentrations, after adding electrolytes, the PPN solution has an osmolality of 800 to 850 mOsmol/L making it difficult to meet the patient's nutritional needs by this route.^{4,7} IV fat emulsions can be added to protein and dextrose solutions, which is referred to as a total nutrient admixture (TNA). TNA provides more total calories while maintaining the same or slightly lower osmolality. However, the caloric density is still low, and relatively large volumes of PPN are required to provide significant amounts of PN. The osmolality of the TNA PPN formulas is still in the 700 to 800 mOsmol/L range, and therefore thrombophlebitis and infiltration of peripheral veins occurs rapidly.^{4,7}

Previously, the standard of care was to flush short peripheral IVs with heparin (10 U/mL) when not in use to maintain patency. However, the results of 2 meta-analyses showed that heparin flushes do not significantly prolong duration of patency or decrease phlebitis rates, and flushing with heparin is more costly than flushing with normal saline.^{9,10} Therefore, present-day practice is to flush with normal saline.

The advantages and disadvantages of short peripheral IV catheters and a comparison with other short-term VAD are shown in Table 1. Advantages include the low cost, ease and rapidity of insertion by nursing personnel, minimal care and maintenance, and low risk of severe life-threatening complications such as catheter-related sepsis. The disadvantage is the high incidence of phlebitis and infiltration, which limits use of these catheters for PN to usually <5 days, in which case PN may not really be needed. In addition, the amount of nutrients that can be provided is limited and the administration of a large amount of IV fluid is required.

Finally, some IV therapies cannot be administered through a peripheral IV because of their pH, osmolality, or inherent toxicity to the veins.

Midline Catheters

Midline catheters are inserted into 1 of the veins in the antecubital fossa, usually the basilic or cephalic vein, and extend for 3 to 8 inches inside the vein (Fig. 2). However, it does not extend to the level of the axillary vein, so it is peripheral IV access and not central venous access. Insertion can be performed using a catheter-over-the-needle technique, by insertion through a tear-away introducer sheath technique, or by the Seldinger technique. X-ray confirmation of tip placement is not necessary. Most midline catheters are made of silicone or polyurethane.

Because the tip of the catheter is placed in a larger vein, midline catheters have a lower incidence of phlebitis and infiltration than the short peripheral IV catheter. Midline catheters also have a lower incidence of infection and are less costly than CVC. Clinical studies have shown that midline catheters last a median of 7 days, with some lasting as long as 49 days.¹¹⁻¹³ Based on the results of these studies, midline catheters can be used safely for up to 2 weeks; however, the optimal duration of the catheter has not been conclusively shown.⁶ All of these studies focused on IV antibiotics and other IV therapies and did not include patients receiving PPN.

The indications, contraindications, and complications for midline catheters are similar to those of the short peripheral catheters. The advantages and disadvantages of midline catheters and a comparison with other short-term VAD are shown in Table 1. Although midline catheters may last longer than short peripheral IV catheters, their use for administering PPN has not been studied. In addition, midline catheters are more expensive than short peripheral IV catheters and require more training for insertion.

Central Venous Catheters

CVC insertion through the SCV was first described by Wilson et al in 1962.¹⁴ Prior to this time, CVC were inserted through 1 of the antecubital veins and threaded up into the central veins, or catheters were inserted through the femoral vein into the inferior vena cava.¹⁴ Initially, CVC were inserted by using a catheter-through-a-needle device. The vein was cannulated with a 14-gauge needle, and the catheter was threaded through the needle and into the vein. The needle was pulled out of the skin, attached to the hub of the catheter, and covered with a hard plastic protective device.¹⁴ However, there was a substantial risk of lacerating the blood vessels and causing bleeding or puncturing the pleura and causing pneumothorax. As a result, the catheter-through-a-needle devices were replaced by the Seldinger technique. This involves cannulating

Table 1
Comparison of advantages and disadvantages of various short-term VAD

VAD	Advantages	Disadvantages
Short peripheral catheter	Easily inserted by nurse or other trained personnel Least expensive Minimal care and maintenance Risk of catheter-related sepsis very low	Only lasts for 48 to 72 hours so site must be changed frequently Risk of phlebitis high Patient may not have adequate peripheral veins Can not instill hyperosmolar solutions so can only use peripheral PN which is limited in amounts of protein and calories and requires increased fluid volume to give even maintenance amount of nutrition Can not instill acidic solutions or medications which cause severe phlebitis
Midline catheter	Same as short peripheral catheter except that the midline catheter may last 3 to 5 days longer (but this has not been proven when used for peripheral PN)	Same as short peripheral catheter Increased cost compared to short peripheral catheter Requires specially trained nurse to insert
CVC	Insertion success rate high even in patients with poor peripheral veins with relatively low complication rate Available in single, double, and triple lumens Can be used for blood drawing and administration of medications, blood, and/or central PN	Insertion risks of hemothorax, pneumothorax, bleeding, injury to surrounding arteries or nerves, and cardiac arrhythmias Risk of complications of catheter-related infection and venous thrombosis Requires physician experienced in CVC insertion More costly than other methods of short-term VAD
PICC	No risk of pneumothorax or puncture of internal carotid or subclavian arteries as with CVC Can be inserted at the bedside Can be inserted by specially trained nurses Easy to remove by nursing personnel Available in single, double and triple lumens External portion can be repaired if torn or damaged Lower risk of catheter-related infection than CVC Insertion is less costly than CVC Can be used for short or long-term venous access	Smaller and longer catheter than CVC so more prone to occlusion and may be more difficult to draw blood Usually not sutured and location on the arm increases the risk of dislodgement Patient may not have adequate veins and insertion is unsuccessful in up to 25% of the attempts Higher rate of coiling and malposition of catheter than CVC Risk of vein thrombosis (probably similar to CVC)

VAD, venous access devices; PN, parenteral nutrition; CVC, central venous catheter; PICC, peripherally inserted central catheter.

the vein with an 18-gauge needle through which a guidewire is inserted. The needle is then completely removed, and after making a small incision in the skin, a vein dilator is passed over the guidewire to dilate the vein. The catheter is then threaded over the guidewire and into the vein, and the guidewire is removed. The 3 most common sites for CVC insertion are the SCV, IJV, and femoral vein (Fig. 1). The external jugular vein can be used for CVC insertion; however, often the acute angle where the external jugular vein empties into the SCV cannot be negotiated with the guidewire or the catheter. The anatomic landmarks and techniques for insertion of CVC into the SCV and IJV have been described in detail elsewhere.¹⁵⁻¹⁷ More recently, ultrasound has been used to assist in CVC placement, especially in patients in whom cannulization of the veins is difficult.¹⁸

Indications for CVC include need for venous access when peripheral access cannot be obtained or when access to the central veins is required. Central

venous access is required for patients who are receiving medications that severely irritate the veins or who require hyperosmolar solutions such as parenteral nutrition, especially if the patient has increased nutrient requirements or cannot tolerate large amounts of fluid. There are no absolute contraindications for CVC, but relative contraindications include the presence of coagulopathy, open wounds or burns on the chest, and tracheostomy.

CVC have a reported complication rate of more than 10%. It has been estimated that 52% of these complications are related to the technique of insertion, 12% are associated with device failure, 6% are related to patient's actions or pathophysiologic events, and 30% are indeterminable.¹⁹ In 1988, the Food and Drug Administration (FDA) formed a task force called the CVC Working Group, which consisted of 45 to 50 individuals from 23 professional medical and nursing associations, 11 manufacturers, 2 universities, and 4 government agencies, including the FDA.¹⁹ The Working Group and its

subcommittees held multiple meetings between 1988 and 1992 with the task of reviewing all aspects of insertion, care, and maintenance of CVC and making recommendations to minimize the complications of CVC. The findings and recommendations of this group were presented at national meetings, published in journal articles, and distributed in an educational videotape series designed for nurses and physicians.¹⁹

CVC complications can be divided into early (those that occur with insertion) and late complications. The early complications include pneumothorax, hemothorax, hydrothorax, bleeding, air embolism, cardiac tamponade, arrhythmia, arterial injury, nerve injury, and catheter misplacement.^{15,20,21} Pneumothorax is most often related to the SCV insertion site. It occurs less frequently when the IJV is used and is nonexistent when the femoral vein is used as the insertion site. Frequently, inexperienced individuals will use the femoral site to avoid causing a pneumothorax; however, the femoral site has increased risk of infection and possibly venous thrombosis compared with the SCV. Therefore, the Centers for Disease Control (CDC) recommends the SCV as the preferred site for CVC insertion.⁶

The reported incidence of pneumothorax ranges from 0.2% to 6.0% and is dependent on the experience of the physician inserting the CVC.^{15,20-23} If the pneumothorax is small (<15% of lung volume), and the patient is asymptomatic and not on positive pressure ventilation, the patient can be observed for clinical signs of respiratory distress. Also, serial chest xrays should be obtained to assess any change in size of the pneumothorax. However, if the pneumothorax is large, symptomatic, or increasing in size or the patient is on positive pressure ventilation, a chest tube should be inserted for evacuation of the pneumothorax. The chest tube can usually be removed within 2 to 3 days once the air leak seals unless the patient is still receiving positive pressure ventilation receiving positive pressure ventilation or has a persistent air leak.¹⁵

Bleeding can occur if there has been unintentional laceration or puncture of an artery or vein during insertion, especially if the patient has an underlying coagulopathy. If there is also a tear in the pleura, blood can collect in the pleural space, causing a hemothorax. Infusion of IV fluids through a CVC that is inadvertently placed in the pleural space can also result in hydrothorax if the cannulation needle, dilator, or introducer sheath perforates the posterior wall of the vein. Therefore, it is important to be able to aspirate blood freely from all lumens once the CVC is in place. Chylothorax may also occur, especially when attempting to insert a CVC into the left SCV, because the thoracic duct, which drains the lymph fluid from the lower body and empties it into the SCV, is in the general area and can be injured. If the hemothorax, hydrothorax, or chylothorax is small, the patient can be observed

with serial chest-x rays. Otherwise, a chest tube should be inserted. If the blood loss is great, ongoing, or if the patient is unstable, exploratory thoracotomy or thoracoscopy may be necessary; but this is very rare.¹⁵ Subcutaneous hematoma or external bleeding at the insertion site usually results from laceration of a small subcutaneous blood vessel and can usually be treated with elevation of the head of the bed to 60 degrees and application of compression dressing.¹⁵ Sandbags can also be placed over the top of the dressing to add direct pressure.

Air embolism is a very rare but potentially fatal complication of CVC insertion.^{15,20} It occurs when a large-bore catheter or introducer is within the vein, and the external end is not clamped or occluded. When the patient inhales, negative intrathoracic pressure sucks air into the venous circulation. If enough air accumulates in the right ventricle, the outflow tract can become blocked, and shock and cardiac arrest may ensue. This can be prevented by keeping the patient in Trendelenburg position (head down) so that venous pressure forces blood out of the catheter rather than sucking air into the catheter. Great care should be taken to keep open ends of catheters or introducer sheaths covered. Air embolus is treated by placing the patient in the left lateral decubitus position, with the left side down and in Trendelenburg position to trap air in the tip of the right ventricle away from the outflow tract. The CVC can then be advanced into the right ventricle in an attempt to aspirate the air out of the heart.¹⁵

Cardiac arrhythmias, most commonly premature ventricular beats or ventricular tachycardia, commonly occur during CVC insertion, usually as a result of the guidewire being advanced into the right ventricle and causing irritation of the wall of the ventricle. Once the guidewire is pulled back into the atrium or superior vena cava, the arrhythmia stops. Rarely, a guidewire, dilator, or introducer sheath can perforate the atrium, ventricle, or intrapericardial portion of the superior vena cava and cause bleeding into the pericardial space, with tamponade, shock, and cardiac arrest. Pericardiocentesis or an emergency pericardial window can be life saving. Infusion of hypertonic PN through a CVC imbedded into the wall of the right ventricle has resulted in right ventricular infarction.¹⁵

Arteries adjacent to the central veins, most commonly the internal carotid and subclavian arteries, can be inadvertently cannulated or lacerated. Arterial cannulation should be suspected if blood return appears unusually bright red following cannulation of the blood vessel. This sometimes occurs with venous blood if the patient is being mechanically ventilated and well oxygenated. Pulsatile blood return will be noticed when the syringe is disconnected from the needle. If this occurs, the needle can be removed, and local direct pressure can be applied. If the patient is coagulopathic or the artery is

tangentially lacerated, surgical repair may be needed.¹⁵

Nerve injury is a rare complication of CVC insertion. However, the brachial plexus, phrenic, vagus, recurrent laryngeal, and cervical sympathetic nerves can all be inadvertently punctured or lacerated by the insertion needle or introducer sheath or may be compressed by a hematoma formation. This could result in pain, numbness, or weakness of the upper extremity, hoarseness, paralysis of the diaphragm, or autonomic nervous system dysfunction. The defect could be temporary if the nerve is contused, partially lacerated, or compressed by hematoma. It may be permanent if the nerve is completely severed.¹⁵

The ideal placement of the tip of a CVC is at the junction of the superior vena cava and the right atrium. However, malposition occurs in 5% to 10% of CVC insertions.¹⁵ Most commonly, an SCV CVC will traverse up the ipsilateral IJV or across to the contralateral SCV instead of curving down into the superior vena cava. The CVC can be inserted too far, and the tip may reside in the right ventricle or the right atrium, or it may extend through the right atrium and down into the inferior vena cava.⁵ A malpositioned CVC increases the risk of venous thrombosis, which will be discussed later. Therefore, chest x-ray confirmation of CVC placement is mandatory.^{19,24-26}

If the CVC is partially occluded or malfunctioning, it can be exchanged over a guidewire, maintaining the same site and avoiding a new puncture site, with its inherent risks. Four studies analyzed the necessity of obtaining a chest x-ray for line placement following guidewire exchange. The combined results of these studies revealed that only 3 of 1801 (0.2%) of the CVC were not in the superior vena cava.²⁷⁻³⁰ All 3 malpositioned CVC occurred in the same study, and all were inserted into the SCV, with 2 of the catheters tips ending up in the contralateral SCV and 1 ending in the ipsilateral IJV.²⁷ All 4 authors concluded that postprocedure chest x-ray is not indicated after a guidewire exchange and that chest x-rays unnecessarily increase the cost of the procedure. One of these studies was published in 1996 and the remainder in 1998, so this information is recent and has not been fully accepted as of yet. The most current FDA¹⁹ and IV Nursing Society²⁵ standards still mandate chest x-ray confirmation of CVC line placement before using the catheter and do not differentiate new insertion from guidewire exchange. Their stance is that no case of catheter malposition is acceptable.

Late complications include catheter dislodgement or occlusion, venous thrombosis, and catheter-related infections.^{15,20,21} A variety of techniques have been used to secure CVC in place; most are based on some method of suturing the catheter to surrounding skin. Despite this, patients and health care workers can inadvertently partially or totally pull out the catheter. Catheter occlusion usually devel-

ops because a fibrin sheath or plug develops at the catheter tip, as previously described, or from inspissation of blood into the end of the catheter. Inability to withdraw blood from the catheter or increasing resistance to infusion or flushing of the catheter are early signs of impending catheter occlusion. Fibrinolytic agents can frequently be used to regain patency and salvage the CVC.¹⁵ Use of fibrinolytic agents will be discussed further in Part II, long-term venous access devices that will be published in the June issue.

The superior vena cava is the optimal location for infusion of hypertonic or irritating drugs because of maximal blood flow rate and volume for dilution outside of the heart, which is proportional to vein diameter. The maximum vein diameter has been measured at 6 mm for cephalic vein, 8 mm for basilic vein, 16 mm for axillary vein, 6 to 19 mm for SCV, and 20 to 30 mm for superior vena cava.⁴ This is 1 of the main reasons that blood flow in the superior vena cava averages 2.0 to 2.5 L/min compared with 150 to 250 mL/min in the forearm veins.⁴ Thrombophlebitis of the veins in the thorax is not shown by skin changes of edema and erythema, as can be observed in catheters inserted through peripheral veins, but rather manifests itself as venous thrombosis. Thrombosis of the IJV, SCV, or superior vena cava is often asymptomatic as a result of extensive collateral circulation.⁴ Catheter-related stenosis or thrombosis of central veins occurs more commonly than previously thought, with a reported incidence of 0.25 episodes per 1000 access days.¹⁵

A study by Mermel recommended that CVC lumens be maintained when not in use by flushing with 100 U/mL of heparin.³¹ In 1998, Randolph et al³² published a meta-analysis that showed that heparin significantly decreased CVC-related venous thrombosis and catheter colonization. It also showed a decrease in catheter thrombus or fibrin sheath and catheter-related bloodstream infection (CR-BSI); however, these differences did not reach statistical significance. These 2 studies focused on giving heparin subcutaneously or as an additive to the infused IV fluid, and not as a heparin flush. Only 1 published study has focused on heparin *versus* normal saline flushes of CVC.³³ It was a nonrandomized study involving cancer patients undergoing apheresis collection for peripheral blood stem cells. The incidence of slow apheresis rate, use of thrombolytics, and radiographic evidence of catheter thrombosis was not significantly different between patients in whom heparin was used and those in whom normal saline flushes were used. Not only does using heparin for CVC flushes increase the cost but there is also concern about heparin-induced thrombocytopenia (HIT) syndrome, which can cause serious morbidity and even mortality.³⁴

The use of heparin flush was first proposed to prevent coagulation of small amounts of blood that reflux into the tip of the CVC as a result of the slight negative intraluminal pressure gener-

ated by pulling the needle out of the cap at the end of the catheter. New CVC caps are available that result in positive pressure as the syringe is removed from the cap, avoiding this reflux phenomenon and obviating the need for heparin flush. One small, nonrandomized study showed that the positive pressure caps reduced catheter occlusion rates from 3% to 1%, but the statistical significance of this difference was not stated.³⁵ Further study is needed to determine the most cost effective CVC caps and flushing protocols.

Catheter-related infection includes local and systemic infections and colonization of the catheter. Local infection, referred to as exit site infection, is defined as erythema, tenderness, induration, or purulence within 2 cm of the CVC skin exit site and accounts for 17% to 45% of CVC-related infections.³⁶ Colonization of the CVC is present if the catheter is removed or exchanged over a guidewire, and the subcutaneous or IV portion of the catheter is cultured and grows >15 CFU of microorganisms and the patient has no systemic signs of sepsis.³⁶ Systemic infection, CR-BSI, is the most severe and costly catheter-related infection. CR-BSI is diagnosed when the line tip culture and a peripheral blood culture grow the same microorganism and the patient has systemic signs and symptoms of sepsis, including fever, leukocytosis, or tachycardia, and there is no other identifiable source for the infection.³⁶

Approximately 180,000 CR-BSI occur each year in the United States.³⁶ The incidence of CVC-related infection ranges from 3% to 20% in hospitalized patients, with rates 2 to 5 times higher in critically ill patients.⁴ CR-BSI occurs in 3% to 7% of CVC.^{20,37} However, with proper technique, care, and maintenance, CVC can be used with a relatively low risk of CR-BSI, even in a high-risk population such as patient with HIV/AIDS.³⁸ The National Nosocomial Infection Surveillance (NNIS) System monitors all types of infections in intensive care units (ICU) and has shown an average rate of CR-BSI anywhere from 4.5 per 1000 catheter days for medical/surgical ICUs to 14.7 per 1000 catheter days in burn ICUs.³⁶ Estimates of the cost of CR-BSI range from \$2800 to \$32,500 per incidence.^{4,36}

Pathogenesis of all types of infections in all types of catheters is by one of the following 4 mechanisms: 1) deposition of microorganisms on the catheter at the time of insertion; 2) migration of microorganisms through the skin and along the catheter; 3) contamination of the catheter hub, tubing junctures, or infusate; or 4) seeding of the catheter from a distant focus of infection.^{4,36,39} In short-term CVC, migration of microorganisms along the external surface of the catheter is probably the most common cause, followed by intraluminal contamination from manipulation of the hub or IV connectors. Seeding from distant focus is uncommon, and contamination of the infusate is exceedingly rare.³⁶ The most common organism associated with CR-BSI is coagulase-

negative staphylococcus, *Staphylococcus epidermidis*, which in 1 study accounted for 33.5% of the organisms. Other organisms and their frequency included *Staphylococcus aureus* (13.4%), *Enterococcus* sp (12.8%), *Candida albicans* (5.8%), *Enterobacter* sp (5.2%), and others (29.3%).³⁶ With the frequent use of multiple antibiotics, many of these bacteria are becoming resistant, most notably methicillin-resistant *S aureus* (MRSA) and vancomycin-resistant enterococci (VRE). *Candida* sepsis is also on the rise and has a 30% to 60% mortality rate.³⁶

Development of CR-BSI depends on 3 interrelated factors: the intrinsic virulence of the organism, patient-specific factors, and catheter-specific factors. Patient-specific factors include the extremes of age (<1 year old and >60 years old), altered host defenses, severity of underlying illness, and presence of distant site infections. Catheter-related factors include thrombus formation around the catheter, CVC insertion site, experience of the inserting physician, and type of catheter.³⁶

CR-BSI strongly correlates with thrombus formation around the CVC. In a series of 94 CVC, Stillman et al⁴⁰ found that 27% of CVC with grossly visible thrombus on the catheter were culture positive, and all of the catheters free of thrombus were culture negative. Raad et al⁴¹ studied 72 patients with cancer who had indwelling CVC and correlated the postmortem autopsy findings with the premortem incidence of CR-BSI. Seven of the 31 patients (23%) with catheter-related thrombosis had experienced CR-BSI compared with none of the 41 patients who had no evidence of thrombosis. Another study found a 2.6-fold increased risk of CR-BSI in patients with catheter-related thrombosis.⁴²

There are no prospective, randomized, clinical trials assessing the influence of site of CVC insertion on catheter-related infection. Further, the definition of catheter-related infection varies from study to study. However, despite this, the literature overwhelmingly reveals a correlation between the site of CVC insertion and subsequent catheter-related infections.

Several studies have compared SCV and IJV insertion sites with regard to catheter-related infections. Ten of 11 studies showed a lower incidence of CVC colonization when the insertion site was the SCV compared with the IJV; however, this difference did not reach statistical significance in 2 studies.⁴³⁻⁵² One study showed a significantly lower incidence of colonization with the IJV site (13% versus 27%, $p < .05$).⁵³ This study did not randomize the site of CVC insertion but did randomize the patients to site care with or without topical antibacterial ointment. The site care did not appear to affect the colonization rate; however, subgroup analysis by insertion site was not performed, and this could have affected the results. Two^{54,55} out of 3 studies demonstrated a significantly lower incidence of CR-BSI with the SCV site compared with the IJV site,

but the other study⁵² showed no significant difference. However, in the latter study, the SCV CVC had a higher mean number of days inserted (11.4 days *versus* 9.7 days).⁵² The increased incidence of colonization and CR-BSI associated with IJV CVC may be the result of increased moisture and therefore increased amounts of bacterial flora in the neck, the difficulty in maintaining an occlusive dressing on the neck, and the closer proximity to contaminated respiratory and oral secretions.

Several studies have compared the SCV and femoral vein insertion sites with regard to catheter-related infections. Two prospective studies have advocated that the femoral vein is a safe and effective site for CVC insertion.^{56,57} The first study⁵⁶ involved 150 femoral CVC inserted in a medical/surgical ICU for a mean duration of 6.4 days (range 1 to 30 days), with no episodes of CR-BSI. This is much lower than the incidence reported by the NNIS. The incidence of other catheter-related infections and deep vein thrombosis (DVT) was not reported. The other study included 80 femoral CVC in a medical/surgical ICU.⁵⁷ CR-BSI, catheter colonization, and femoral DVT occurred in 3.7%, 13.7%, and 8.5% of the patients, respectively. However, neither of these studies included a control group of SCV CVC.

Five^{45,46,49,52,58} of 7 studies demonstrated a significantly lower incidence of catheter colonization associated with the SCV site compared with the femoral site, and 2 other studies^{50,59} showed no significant difference. One of these 2 later studies involved burn patients, and the CVC was routinely changed to a new site every 48 hours.⁵⁹ The incidence of catheter colonization was 8% for the femoral CVC and 14% for the nonfemoral CVC. The incidence for CR-BSI was 3% for femoral CVC and 1% for the nonfemoral CVC. If the catheters had been left in for a longer period of time, which is the usual routine, the incidence of catheter-related infection may have been different between the 2 groups. Also, the nonfemoral CVC group included SCV and IJV insertion sites, so this was not a fair comparison. The other study involved critically ill children, and only the rates of colonization and not the raw data were presented.⁵⁰ The increased incidence of colonization and CR-BSI associated with femoral CVC may be related to the increased moisture and therefore increased quantity of bacterial flora in the groin area. The CDC recommends that the SCV as the preferred site for CVC insertion.⁶

The level of experience of the physician inserting the CVC may influence the risk of catheter-related infection. One prospective study showed that physicians who had placed <50 CVC had a twofold higher incidence of CR-BSI compared with more experienced physicians.²¹ Properties of the catheter itself can effect the risk of infection. Some materials promote microbial adherence more than others do. Some materials are also more thrombogenic, and as discussed earlier, thrombus is strongly associated

with CR-BSI. Catheter materials in decreasing order of thrombogenicity are polyvinyl chloride, polyethylene, polyurethane, and silicone.³⁶

PN, with its increased glucose content, is a prime medium for bacterial growth and spread. Therefore, to decrease the risk of infection, PN should be administered through a dedicated venous access that is not used for any other purpose. However, many patients receiving PN require multiple other IV therapies and often this results in problems with incompatibility. For these reasons, CVC with multiple, dual or triple, lumens have been designed. One lumen can be dedicated for PN use, and the other lumens can be used for other IV therapies. The internal openings of the lumens are usually staggered about 2.5 cm apart so that incompatible medications or solutions can be infused simultaneously through separate lumens.

Studies comparing the catheter-related infection rates for single- and multiple-lumen CVC have been contradictory. Four prospective, randomized, controlled trials have compared CR-BSI for single-lumen *versus* multilumen CVC. Two of these studies concluded that multilumen CVC increased the risk of CR-BSI. One study⁶⁰ showed a statistically significant difference in CR-BSI (2.6% *versus* 13.1%, $p < .01$), whereas the difference in CR-BSI rates in the other study⁶¹ did not quite reach statistical significance (0% *versus* 12.8%, $p = .055$). Possible reasons why multilumen CVC might increase the risk of catheter-related infection are the increased trauma to the vein from the larger-sized catheter and the more frequent manipulation of the multiple catheter hubs.³⁶ The other 2 studies concluded that the number of catheter lumens does not significantly effect the incidence of CR-BSI. One of these studies⁶² defined CR-BSI on the basis of clinical signs and qualitative catheter tip cultures (8.9% $\frac{7}{68}$ for single-lumen *versus* 11.5% $\frac{7}{61}$ for triple-lumen, $p = .62$) and by quantitative catheter tip cultures (16.2% for single-lumen *versus* 11.5% for triple-lumen, $p = .44$). In addition to the CVC, 37% of the single-lumen group required peripheral venous access compared with only 1.6% (1 patient) in the triple-lumen group. The other study randomized patients to double-lumen or triple-lumen CVC and compared the CR-BSI of these patients with the occurrence of CR-BSI in single-lumen historical controls from the same institution.⁶³ There was no significant difference among the 3 groups (1.9% for triple-lumen, 2.0% for double-lumen, and 1.4% for single-lumen). Although, ideally, PN should be administered through a dedicated single-lumen CVC, many of these patients require venous access for other reasons (ie, administration of medications or blood drawing). Therefore, multilumen CVC are acceptable access devices for PN, but the lumen used for PN should be a "virgin" port dedicated to PN use only. If a CVC is already in place when PN is initiated but has already been used for other IV therapies, the CVC can be exchanged over a guide-

wire, and the new catheter can be used for PN as long as the culture of the old CVC tip remains negative.⁶⁴

Treatment of catheter-related infections in short-term CVC depends on the type of infection. If there is mild erythema at the skin exit site, local measures such as more frequent site care and warm compresses can be tried. However, if there is no improvement or if there is purulent drainage at the exit site, the CVC needs to be removed and, if still needed, inserted into a new site.³⁶

If the patient has systemic signs of sepsis, fever, or leukocytosis, CR-BSI should be suspected. Blood cultures should be drawn through the catheter and from a peripheral site, and all other potential sources of infection should be cultured or evaluated. The CVC should be removed and reinserted at a new site or exchanged over a guidewire at the same site. The tip of the old CVC should be cut off and sent to the laboratory for culture. Michel et al⁶⁵ conducted a prospective study of 146 patients with a CVC. Forty-one (28%) of these patients were suspected of having CR-BSI and were randomized to either guidewire change or removal and reinsertion at a new site. There was no significant difference in catheter contamination rates between the 2 groups, and the guidewire group had fewer complications with reinsertion. Only 7% of the patients suspected of having CR-BSI were subsequently proven to have infection. Another study showed that only 24% of the 63 CVC suspected of causing CR-BSI were actually infected.²³ Therefore, these and other authors advocate guidewire exchange rather than insertion at a new site for patients with suspected CR-BSI as long as there is no evidence of infection at the skin insertion site.^{23,64,66,67} If the CVC has been changed over a guidewire, and the tip culture is positive (>15 CFU), the line should probably be removed and, if still needed, inserted in a new site. However, 1 study showed that as long as the blood cultures were negative and the patient had no systemic signs of infection, repeated guidewire changes could "sterilize" the CVC.⁶⁶ Systemic antibiotics are only necessary if the peripheral blood culture is positive, in which case the sepsis requires a standard 2-week course of antibiotics.³⁶

Factors that may help decrease the incidence of catheter-related infections include maximal barrier precautions on insertion of CVC, proper selection and use of antiseptics, routine and appropriate care of the catheter site and hubs, the appointment of specially trained and designated personnel responsible for CVC insertion and maintenance, proper catheter surveillance, and modifications in the CVC themselves.

Maximal barrier precautions include the physician wearing a surgical hat and mask and sterile gown and gloves when inserting the CVC, adequately preparing the site with antiseptic, and draping the site in a sterile fashion.^{6,36} Use of these measures significantly decreases the incidence of

catheter-related infection and is even more important than where the procedure is performed. Raad et al⁶⁸ randomized patients receiving a CVC to a study group in which maximal barrier precautions, as outlined above, were used or to a control group in which only sterile gloves and small drape were used. The study group had a significantly lower incidence of catheter-related infection (2% $4/176$ versus 7% $12/167$, $p < .05$). Mermel et al⁴⁸ conducted a prospective, observational study to identify the pathogenesis and epidemiology of catheter-related infections associated with 297 pulmonary artery Swan-Ganz catheters. The majority of these catheters (69%) were inserted in the operating room with the physician wearing only a sterile mask and gloves and using a small drape, and the remainder were inserted in the ICU with the physician wearing a mask, sterile gown and gloves, and using a large drape. Multivariate analysis revealed that catheter-related infections were associated with colonization of the skin at the catheter insertion site, insertion into the IJV versus the SCV or femoral vein, duration of catheter > 3 days, or insertion in the operating room using less stringent barrier precautions. The catheters inserted under maximal barrier protection had a significantly lower incidence of catheter-related infection (15% versus 25%, $p < .01$). PN was administered through Swan-Ganz catheters in 18% of the patients, and it did not seem to be correlated with catheter-related infection. CDC guidelines advocate the use of maximal barrier precautions during CVC insertion.⁶

Iodophors are the most common antiseptics used in the United States for a variety of sterile preparations, including preparation for CVC insertion. However, iodophors have relatively weak antiseptic properties. Maki et al⁶⁹ conducted a prospective, randomized, controlled trial comparing 3 different antiseptics (2% aqueous chlorhexidine, 10% povidone-iodine, and 70% alcohol) and found that chlorhexidine had an 84% lower incidence of CR-BSI than the other 2 antiseptics. Although chlorhexidine is widely used in Europe, it has only recently been approved for use in the United States.^{6,36} Studies on the use of antimicrobial ointments at the CVC insertion site have been inconclusive and contradictory, and at present, their use is not recommended; however, further studies in this area are needed.^{6,36}

Routine cleansing of the skin with an antiseptic and occlusive dressings have been used in an attempt to decrease microbial growth and colonization at the CVC skin insertion site.^{6,36} Sterile gauze and tape were used as the first CVC dressings. In the early 1980s, transparent dressings were developed, which had the advantage of allowing visual inspection of the CVC insertion site daily or more frequently without removing the dressing. However, there were concerns about the decreased permeability of these transparent dressings, which could lead to increased moisture and increased microbial growth and colonization of the skin around the CVC

skin exit site. Newer transparent dressings are now available, which have a high water vapor permeability rating, and these are becoming very popular.^{6,36} Even newer CVC dressings that release antimicrobial agents in an attempt to decrease the microbial colonization of the skin are becoming available.³⁶ With regard to the frequency of CVC dressing changes, the CDC does not recommend a standard interval but rather recommends changing dressing only when clinically indicated. This includes when the CVC is inserted, when it is removed or replaced, or when the dressing becomes damp, loosened, or soiled.⁷⁰

The catheter hub is an important portal for intraluminal CVC contamination and is frequently handled with less-than-optimal aseptic technique.³⁶ The catheter hub should be cleansed with an antiseptic agent such as 70% isopropyl alcohol or 10% povidine-iodine before inserting anything through it or when disconnecting it. The mechanical action of wiping the hub may be almost as important as the antiseptic agent itself.³⁶ Minimizing hub manipulation may decrease the incidence of CR-BSI, and this has led to the proposal of protocols to increase the interval between tubing changes beyond the traditional 24 hours.³⁶ New, disinfecting catheter hubs that incorporate an antiseptic barrier have been developed and have been estimated to reduce hub-related catheter sepsis by >90%.^{36,71} There was also concern that the needleless systems may increase CR-BSI because of the potential for trapping fluids in the injection caps; however, this has not been proven conclusively.^{36,71} Studies have also shown that the use of personnel specially trained or designated with the responsibility for insertion and maintenance of IV devices can significantly reduce the incidence of catheter-related infections and overall costs.⁷²⁻⁷⁴ However 1 study revealed a similar rate of catheter-related infection when ward nurses performed CVC dressing changes as when infusion therapy nurses performed this task, provided that aseptic technique was maintained.⁷⁵

Risk of catheter-related infection correlates with the length of time the CVC is in place, with the incidence beginning to rise after 3 days of insertion. For this reason, initial recommendations were to routinely change the CVC to a new site every 3 to 7 days. However, this subjected the patient to the pain, discomfort, and risk of repeated CVC insertions. Studies comparing routine change to new site with guidewire exchange at the same site found no significant difference in catheter-related infection rates.^{76,77} In 1990, Eyer et al⁷⁸ conducted a prospective study in which 112 ICU patients with CVC, pulmonary artery catheters, or arterial catheters were randomized to 1 of 3 strategies: 1) routinely change the catheter to a new site every 7 days; 2) no weekly changes, but change to a new site if change was required for clinical reasons; and 3) routinely change the catheter over a guidewire at the same site every 7 days. There were no significant differ-

ences in CR-BSI incidence among the 3 groups (16%, 13%, and 15% respectively, $p = .94$). The CDC does not recommend routine CVC changes and recommends change only if catheter-related infection is suspected or proven, or if the catheter is occluded or malfunctioning. The CDC does, however, recommend changing pulmonary artery Swan-Ganz catheters and arterial catheters every 5 days.⁷⁰ Guidewire exchanges are safe and decrease the risk of new insertion when changing from a CVC to a pulmonary artery Swan-Ganz catheter or *vice versa*, when all ports of the CVC have been previously used and an unused line is needed for PN, or when the CVC is malfunctioning or partially occluded.^{64,66}

Several catheter modifications have been tried to decrease the incidence of catheter-related infections. In 1988, Maki et al³⁷ first reported clinical results using a silver-impregnated collagenous cuff with CVC insertion. The cuff is attached to the proximal end of the catheter. Once the catheter is in place, the cuff is slid down the catheter and inserted under the skin around the subcutaneous portion of the catheter. Subcutaneous tissues grow into the cuff, anchoring the catheter in place and acting as a mechanical barrier to migration of bacteria along the surface of the catheter. The silver ions in the cuff provide an additional chemical barrier to bacterial migration. The cuff is biodegradable and disappears after 2 to 3 weeks.

Four prospective, randomized, controlled trials have analyzed the effect of this silver-impregnated cuff on CR-BSI and catheter colonization.^{37,79-81} All 4 trials showed a lower incidence of catheter colonization with the cuffed catheter; although the difference did not reach statistical significance in 2 studies.^{79,81} Combining the results of these 4 studies revealed a significantly lower incidence of catheter colonization with the cuffed catheter (11% [31/272] *versus* 23% [81/353], $p < .001$). A decreased incidence of CR-BSI was shown with the cuffed catheter in 2 of the 4 studies, but the differences did not reach statistical significance.^{37,80} The other 2 studies showed no difference in the incidence of CR-BSI between the cuffed and control catheters.^{79,81} Combining the results of the 4 studies, the CR-BSI rate associated with cuffed CVC was about half that for noncuffed catheters (2.2% *versus* 4.2%, $p = .16$). However, the incidence of CR-BSI was low in both groups, and a much larger sample size would be needed to reach statistical significance.

The silver-impregnated cuff has been used in 2 other prospective, randomized studies.^{22,82} One of these studies randomized patients to either standard CVC, with the line changed to a new site every 7 days, or cuffed CVC, which was changed to new site every 14 days.²² Overall, 52% of the patients required CVC for longer than 7 days, and 22% required at least 1 CVC change. The incidence of CR-BSI was 6.8% and was not significantly different between the 2 study groups. The authors concluded that the silver-impregnated cuff permitted extended

access up to 14 days, with no increase in CR-BSI and a decrease in insertion complications with repeated new sticks.

The other study randomized patients to 3 groups.⁸² One group received a silver-impregnated cuffed catheter with semioclusive dressing; the second group received a noncuffed, tunneled CVC (at bedside CVC tunneled through the subcutaneous tissues to increase the distance between the skin exit site and where the catheter enters the vein) with semioclusive dressing; and the third group received a noncuffed, tunneled CVC with the skin exit site covered with collodion (liquid when applied then dries to seal off the wound). There were 50 patients in each of the 3 groups. There was no significant difference among the groups with regard to CR-BSI (0%, 2%, and 0%, respectively, $p = .37$) or insertion site infections (2%, 2%, and 0%, respectively, $p = .60$). However, this was a small study, with a very low incidence of catheter-related infection, and the study groups differed by presence of the cuff, presence of tunneling, and type of dressing. Therefore, it is difficult to interpret these results.

Various antibiotics have been bonded to CVC in an attempt to decrease catheter-related infections. In 1991, a prospective, randomized study by Kamal et al⁸³ studied patients receiving either CVC (93 catheters) or arterial catheters (85 catheters). Patients received either standard catheters or catheters treated with a bonding agent followed by cefazolin such that the antibiotic was bonded to both the internal and external surface of the catheter. There were no cases of CR-BSI in either group. The antibiotic-bonded CVC had a significantly lower incidence of colonization (2% [2/97] versus 14% [11/81], $p < .01$), and there were no differences in rate of site infection (7% versus 6%).

In the early 1990s, a new polyurethane CVC in which the external surface was impregnated with chlorhexidine and silver sulfadiazine (CH/SS) was developed.⁸⁴ Chlorhexidine is a potent antiseptic that has been used widely throughout the world for cutaneous disinfection, handwashing, oral care, irrigation of surgical wounds, peritoneal irrigation, urinary bladder irrigation, vaginal douche, burn wound treatment, and as part of most water-soluble medical lubricants.⁸⁴ Silver sulfadiazine is a stable combination of the antiseptic silver and sulfadiazine, which is a potent bactericidal and fungicidal agent used worldwide for treatment of burn wounds to prevent infection.⁸⁴

In 1999, Veenstra et al⁸⁵ published a meta-analysis of 13 prospective, randomized, controlled trials^{84,86,97} carried out between 1994 and 1998, which compared the incidence of CVC colonization or CR-BSI between CH/SS coated and uncoated catheters. Three other studies were not included in the meta-analysis; 2 of these were published in 1997,^{98,99} and 1 was published in 1999.¹⁰⁰ Fourteen of the 16 studies reported colonization rates and all showed a lower incidence of colonization with antibiotic-

coated CVC; although in 4 of the studies, the differences did not reach statistical significance. Combining the results of these studies, the antibiotic-coated CVC had a significantly lower colonization rate than the uncoated catheters (16% [231/1421] versus 29% [405/1416], $p < .001$). Fourteen studies compared the incidence of CR-BSI, and only 1 study⁸⁴ of the 16 revealed a significant decrease in CR-BSI with the antibiotic-coated catheter. However, when the results of these studies were combined, the antibiotic catheters had a significantly lower incidence of CR-BSI (3.4% [60/1749] versus 4.9% [87/1760], $p < .05$). Veenstra et al⁸⁵ concluded that the use of CH/SS-coated CVC effectively reduces the incidence of CR-BSI in high-risk patients requiring short-term CVC and may provide a strategy for decreasing the overall incidence and cost of catheter-related infections. They suggested that the decision to use these catheters should be made based on the baseline risk of catheter-related infection in specific patient populations, potential reductions in morbidity and mortality, economic costs, and the risk of adverse events. Severe anaphylaxis associated with the CH/SS-coated catheters has been reported, with some reported deaths.^{85,101} Yasukawa et al¹⁰¹ reported 12 such reactions out of 170,000 catheters used in Japan, for an incidence of 7.1 reactions per 100,000 catheters inserted.

In the mid-1990s, an antibiotic CVC that was coated on its external and internal surface with minocycline and rifampin (M/R) was developed.¹⁰² Both of these agents are active against methicillin-sensitive and methicillin-resistant *S aureus*, with activity against gram-negative organisms and *Candida* species. These antibiotics are rarely used for treating bloodstream infections, and antimicrobial resistance has not been a problem. Three prospective, randomized, controlled trials have shown that the use of M/R-coated CVC decreased the incidence of colonization and CR-BSI compared with uncoated CVC.^{100,102,103} However, these differences reached statistical significance in only 2 studies for colonization rate and in 1 study for CR-BSI. Combining the results of these 3 studies demonstrates the superior results with the M/R-coated CVC with regard to the incidence of colonization (8% [15/188] versus 27% [53/195], $p < .01$) and CR-BSI (0% [0/188] versus 5% [10/195], $p < .01$).

Raad et al¹⁰⁴ compared the CH/SS-coated and M/R-coated CVC *in vitro* and *in vivo* in a rabbit model. The half-life of the inhibitory activity of the M/R CVC *in vitro* was much longer than the CH/SS CVC (25 days versus 3 days). In the *in vivo* rabbit model, the M/R-coated CVC had a significantly lower rate of colonization and infection compared with the CH/SS-coated CVC. Two prospective, randomized, controlled trials have compared the M/R- and CH/SS-coated CVC.^{100,105} Both studies showed lower colonization and CR-BSI with the M/R-coated CVC; although the difference was statistically significant in only 1 of the 2 studies. The combined

results of these 2 studies demonstrated a significantly lower incidence of colonization (8% [32/394] versus 23% [94/418], $p < .001$) and CR-BSI (0.3% versus 3.3%, $p < .01$) with the M/R-coated CVC compared with the CH/SS-coated CVC.

The advantages and disadvantages of CVC and a comparison with other short-term VAD for PN are shown in Table 1.

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