Invited Review

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. Of these, 5 million are central venous catheters (CVC) or pulmonary artery catheters. Approximately 500,000 long-term CVC are inserted in the United States annually, mainly for chemotherapy and parenteral nutrition (PN). Although there is no absolute cutoff, long-term CVC are indicated when venous access is required for more than 6 to 8 weeks. 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. 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.

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.
Short Peripheral IV Catheters

Short peripheral IV catheters (1 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.9 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 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 1. Venous anatomy of upper and lower extremity.

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 al3 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...
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

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<tr>
<th>VAD</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Short peripheral catheter</td>
<td>Easily inserted by nurse or other trained personnel</td>
<td>Only lasts for 48 to 72 hours so site must be changed frequently</td>
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<td></td>
<td>Least expensive</td>
<td>Risk of phlebitis high</td>
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<td></td>
<td>Minimal care and maintenance</td>
<td>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</td>
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<td></td>
<td>Risk of catheter-related sepsis very low</td>
<td>Can not instill acidic solutions or medications which cause severe phlebitis</td>
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<tr>
<td>Midline catheter</td>
<td>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)</td>
<td>Same as short peripheral catheter</td>
</tr>
<tr>
<td></td>
<td>Insertion success rate high even in patients with poor peripheral veins with relatively low complication rate</td>
<td>Increased cost compared to short peripheral catheter</td>
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<td></td>
<td>Available in single, double, and triple lumens</td>
<td>Requires specially trained nurse to insert</td>
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<tr>
<td></td>
<td>Can be used for blood drawing and administration of medications, blood, and/or central PN</td>
<td>Insertion risks of hemotorax, pneumotorax, bleeding, injury to surrounding arteries or nerves, and cardiac arrhythmias</td>
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<tr>
<td></td>
<td></td>
<td>Risk of complications of catheter-related infection and venous thrombosis</td>
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<td></td>
<td></td>
<td>Requires physician experienced in CVC insertion</td>
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<td></td>
<td></td>
<td>More costly than other methods of short-term VAD</td>
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<tr>
<td>CVC</td>
<td>Insertion success rate high even in patients with poor peripheral veins with relatively low complication rate</td>
<td>Smaller and longer catheter than CVC so more prone to occlusion and may be more difficult to draw blood</td>
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<tr>
<td></td>
<td>Available in single, double, and triple lumens</td>
<td>Usually not sutured and location on the arm increases the risk of dislodgement</td>
</tr>
<tr>
<td></td>
<td>Can be used for blood drawing and administration of medications, blood, and/or central PN</td>
<td>Patient may not have adequate veins and insertion is unsuccessful in up to 25% of the attempts</td>
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<td></td>
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<td>Higher rate of coiling and malposition of catheter than CVC</td>
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<td>Risk of vein thrombosis (probably similar to CVC)</td>
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<tr>
<td>PICC</td>
<td>No risk of pneumotorax or puncture of internal carotid or subclavian arteries as with CVC</td>
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<td></td>
<td>Can be inserted at the bedside</td>
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<tr>
<td></td>
<td>Can be inserted by specially trained nurses</td>
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<td></td>
<td>Easy to remove by nursing personnel</td>
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<td></td>
<td>Available in single, double and triple lumens</td>
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<td></td>
<td>External portion can be repaired if torn or damaged</td>
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<td></td>
<td>Lower risk of catheter-related infection than CVC</td>
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<td>Insertion is less costly than CVC</td>
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<td>Can be used for short or long-term venous access</td>
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VAD, venous access devices; PN, parenteral nutrition; CVC, central venous catheter; PICC, peripherally inserted central catheter.
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, hemotorax, 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 x-rays 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 hematohorax. 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 hemotorax, 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. Percardiocentesis 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.\textsuperscript{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 confused, partially lacerated, or compressed by hematoma. It may be permanent if the nerve is completely severed.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 FDA\textsuperscript{19} and IV Nursing Society\textsuperscript{25} 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.\textsuperscript{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 develops 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.\textsuperscript{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.\textsuperscript{7} 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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{15}

A study by Mermel recommended that CVC lumens be maintained when not in use by flushing with 100 U/mL of heparin.\textsuperscript{31} In 1998, Randolph et al\textsuperscript{32} 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.\textsuperscript{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.\textsuperscript{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 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. Two54,55 out of 3 studies demonstrated a significantly lower incidence of CR-BSI with the SCV site compared with the IJV site.
but the other study\textsuperscript{52} showed no significant difference. However, in the latter study, the SCV CVC had a higher mean number of days inserted (11.4 days \textit{versus} 9.7 days).\textsuperscript{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.\textsuperscript{56,57} The first study\textsuperscript{56} 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.\textsuperscript{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\textsuperscript{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\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 \textit{versus} multilumen CVC. Two of these studies concluded that multilumen CVC increased the risk of CR-BSI. One study\textsuperscript{50} showed a statistically significant difference in CR-BSI (2.6\% \textit{versus} 13.1\%, \(p < .01\)), whereas the difference in CR-BSI rates in the other study\textsuperscript{61} did not quite reach statistical significance (0\% \textit{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.\textsuperscript{36} The other 2 studies concluded that the number of catheter lumens does not significantly effect the incidence of CR-BSI. One of these studies\textsuperscript{52} defined CR-BSI on the basis of clinical signs and qualitative catheter tip cultures (8.9\% \(\%_6\) for single-lumen \textit{versus} 11.5\% \(\%_6\) for triple-lumen, \(p = .62\)) and by quantitative catheter tip cultures (16.2\% \textit{versus} 11.5\% \(\%_6\) 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.\textsuperscript{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 one (28%) of these patients were suspected of having prossective 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. 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 (2%4/10CFU), the line should probably be removed and, if still needed, inserted in a new site. However, I 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%3/16 versus 7%1/16, 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.5,36 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. Even newer CVC dressings that release antimicrobial agents in an attempt to decrease the microbial colonization of the skin are becoming available. 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.

The catheter hub is an important portal for intraluminal CVC contamination and is frequently handled with less-than-optimal aseptic technique. 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. 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. New, disinfecting catheter hubs that incorporate an antiseptic barrier have been developed and have been estimated to reduce hub-related catheter sepsis by >90%. 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.

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. 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.

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.

In 1990, Eyer et al 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 differences 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. Guide-wire 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.

Several catheter modifications have been tried to decrease the incidence of catheter-related infections. In 1988, Maki et al 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. 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. 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. The other 2 studies showed no difference in the incidence of CR-BSI between the cuffed and control catheters. 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. 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. 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 semiocclusive 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 semiocclusive 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 trials84,86,97 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 199798,99 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-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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