Guidelines on the insertion and management of central venous access devices in adults

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SUMMARY

Central venous access devices are used in many branched of medicine where venous access is required for either long-term or a short-term care. These guidelines review the types of access devices available and make a number of major recommendations. Their respective advantages and disadvantages in various clinical settings are outlined. Patient care prior to, and immediately following insertion is discussed in the context of possible complications and how these are best avoided. There is a section addressing long-term care of in-dwelling devices. Techniques of insertion and removal are reviewed and management of the problems which are most likely to occur following insertion including infection, misplacement and thrombosis are discussed. Care of patients with coagulopathies is addressed and there is a section addressing catheter-related problems.

INTRODUCTION

These guidelines are a review of basic principles and relevant research for medical and nursing staff involved in the care of patients with central venous access devices (CVADs). They complement existing guidelines for nursing staff (RCN, 2005) and are based on database searches using appropriate keywords, and a review of the existing published guidelines written by expert groups [British Committee for Standards in Haematology (BCSH Guidelines, 1997)]. The authors were selected to embrace a wide range of interest in central

Corresponding author belongs to British Committee for Standards in Haematology.

venous access devices, including clinical, haematological, radiological, anaesthetic, critical care and nursing. The guidelines are not intended as a substitute for local policies and protocols but should provide a useful source of reference for those writing such documents. These guidelines relate to the insertion and management of nontunnelled and skin-tunnelled central venous catheters (CVC), apheresis catheters, implanted ports and peripherally inserted central catheters (PICC).

MAJOR RECOMMENDATIONS

Following a review of the current literature, which is fully referenced in the body of the paper, the following recommendations are made.

- Patients should receive clear and comprehensive verbal and written information explaining the risks, benefits and care of the catheter. Signed consent should be obtained prior to catheter insertion.
- Nontunnelled catheters are indicated for short-term use when peripheral venous access is impractical.
- Tunnelled central venous catheters are indicated for the repeated administration of chemotherapy, antibiotics, parenteral feeding and blood products, and for frequent blood sampling. They are recommended for patients in whom long-term (>30 days) central venous access is anticipated.
- Fully implanted catheters (ports) are more suitable for children and for less frequent accessing but long-term use, whereas skin-tunnelled catheters are recommended for intensive access.
- Peripherally inserted central catheters should be avoided for inpatient therapy because of limited catheter longevity and increased incidence of thrombosis. They are more suited to ambulatory or outpatient-based therapy.
- Polyurethane PICC allow easier infusion of blood products as greater flow rates are achieved because the thinner walls provide a larger internal diameter of the catheter. The decision to use polyurethane catheters should be balanced against the higher risk of thrombosis with these catheters compared with silicone catheters.
- The number of lumina and diameter of catheters should be kept to the minimum.
- Experienced operators, regardless of speciality, should perform catheter insertion with training,

supervision and competence assessment programmes in place. Paediatric specialists should insert catheters in children.
- Ultrasound guided insertion is recommended for all routes of central venous catheterization. The use of ultrasound is also recommended for the insertion of PICC when the peripheral veins are not visible or palpable.
- Imaging facilities (fluoroscopy, intravenous contrast studies and standard radiography) should be available for the insertion of skin-tunnelled CVCs and ports.
- Catheter insertion should take place in an operating theatre or similar clean environment. Bedside placement should not be performed except in an emergency, apart from PICC placement.
- Rigorous skin cleansing with a chlorhexidine gluconate 2% in alcohol or aqueous solution is recommended prior to catheter insertion.
- Antibiotic/antimicrobial impregnated catheters, for example, chlorhexidine and silver sulfadiazine impregnated catheters should be considered for appropriate risk groups of patients to minimize infection risk. These are becoming available for tunnelled devices.
- Routine antibiotic prophylaxis is not recommended.
- Flushing with heparin *vs.* normal saline remains controversial.
- Routine replacement, for example, weekly change, of short-term catheters as a means to reduce infection rates is not recommended.
- Guidewire-assisted catheter exchange to replace a malfunctioning catheter is acceptable if there is no evidence of infection. However, if infection is suspected the existing catheter should be removed and a new catheter inserted at a different site. This technique is generally impractical for cuffed tunnelled catheters or ports when it may be technically easier and safer to insert a new catheter into a clean site.
- Dressings should be changed 24 h after catheter insertion and weekly thereafter.
- Securing devices, for example, Statlok™ are preferable to stitches, and lines should not be sewn into or around the vein.
- Needle-free connectors should be used to reduce risk of infection to patients and needle stick injury to staff.

- A positive pressure method of flushing (by protocol, according to the type of catheter) is essential to maintain catheter patency.
- IV therapy giving sets should be changed every 24–48 h if used for transfusing blood products, and every 72–96 h otherwise.
- Pre-existing haemorrhagic, thrombotic, or infective problems must be effectively managed before catheter insertion.
- Blood products may be administered concurrently with another drug/infusion through a dual bore catheter.
- Low-dose warfarin prophylaxis is not recommended, but therapeutic dosing may be required in selected patients at risk of developing a thrombosis.
- Thrombosis and infection must be promptly diagnosed and vigorously treated. Both complications may require removal of the catheter.
- Tunnelled catheters can be pulled out if the cuff has not anchored in the tissues. Otherwise, a cut-down procedure is needed to free the cuff. Ports require surgical removal. All procedures should be undertaken by experienced personnel.
- Units should audit complications associated with central venous catheterization and use the data to develop preventative measures. Close liaison with the local microbiology department is essential to monitor trends in infection.

Indications for catheter insertion

These catheters are indicated (i) when venous access is poor, (ii) when embarking on prolonged intravenous chemotherapy and/or total parenteral nutrition (TPN), or for repeated administration of blood products, (iii) when intravenous therapy involves drugs known to be venous sclerosants, (iv) when ambulatory chemotherapy is to be given as an outpatient, (v) in the situation of repeated sampling, or venesection.

Choice of catheter

Catheters are categorized into (i) nontunnelled catheters, (ii) tunnelled catheters with anchoring cuff, (iii) implanted ports (iv) apheresis/dialysis catheters (tunnelled and nontunnelled) and (v) PICC. They may have single or multiple lumina and can be open ended or valved. Multiple lumina catheters are advantageous in patients undergoing stem cell transplantation or chemotherapy where a number of agents and blood products require simultaneous infusion. Blood products may be administered concurrently with another drug/infusion through a dual bore catheter. Multiple lumina catheters are associated with increased morbidity (Farkas *et al.*, 1992; Dezfulian *et al.*, 2003), but in the haematology setting, the increased risk is likely to be offset by the convenience of multilumina catheters, thereby justifying their use. If TPN is being administered, a single lumen central venous catheter or lumen should be dedicated exclusively to this purpose (Pratt *et al.*, 2001). The smallest diameter catheter should be employed, to minimize the risk of catheter-related thrombosis and/or subsequent venous stenosis (Knutstad, Hager & Hauser, 2003). However, it may be difficult to administer blood products via very narrow lumina.

Nontunnelled central venous catheters

In an attempt to reduce catheter-related blood stream infection (CRBSI) rates, various materials have been investigated. These have been reviewed, and antimicrobial/antiseptic impregnated catheters, for example, chlorhexidine and silver sulfadiazine short-term catheters have been shown to be effective in reducing catheter-related blood stream infections, but other types are commercially available. A large randomized controlled trial showed that CVCs coated with chlorhexidine and silver sulfadiazine were associated with a 44 % reduction in colonization and a 79 % reduction in catheter-related blood stream infection (Maki *et al.*, 1997), although the largest study to date, in which the mean duration of catheterization was 20 ± 12 days, failed to show any benefit (Logghe *et al.*, 1997). The use of antimicrobial/antiseptic impregnated catheters is recommended for adults who require short-term (<10 days) central venous catheterization and who are at high risk of infection (Pratt *et al.*, 2001; Pellowe *et al.*, 2003). The debate continues about such catheters and their propensity for inducing antibiotic resistance, and occasional severe allergic reactions have been reported (Cicalini, Palmieri & Petrosillo, 2004).

Tunnelled catheters

Tunnelled catheters are recommended for patients in whom long-term (>30 days) central venous access is necessary (Pratt *et al.*, 2001). Devices exist with and without Dacron anchoring cuffs. Tunnelled catheters have been shown to be associated with lower infection rates than nontunnelled catheters (Randolph *et al.*, 1998). The cuff induces an inflammatory reaction within the subcutaneous tunnel leading to fibrosis, with catheter fixation usually occurring within 3–4 weeks of insertion. Valved catheters have the advantage of not requiring heparin flushes but may need pressurized infusions to administer blood products. They also tend to be more costly. There is little hard evidence to support one type of catheter over another.

Implanted ports

Ports have been shown to have the lowest reported rates of catheter-related blood stream infections compared with either tunnelled or nontunnelled CVC (Pegues *et al.*, 1992; Groeger *et al.*, 1993). Most ports are single lumen, which makes them more suited to long-term intermittent therapy. They tend to be used more frequently in paediatrics, and in patients with solid tumours (Camp-Sorrell, 1992; Gabriel, 1999). In the adult haematology setting, they may be of use in sickle cell anaemia or thalassaemia, where patients are receiving regular blood transfusions. Ports may also be useful for oncology patients with poor peripheral venous access who are receiving less intensive therapy unlikely to cause prolonged neutropenia. They allow less restricted bathing and swimming and may appeal to patients concerned about the psychological aspects of the presence of the external part of the nonimplanted catheters. They are more expensive to purchase, insert and remove, and they leave larger scars.

Apheresis/dialysis catheters

These can be either nontunnelled (Vascaths™) or subcutaneously tunnelled with a cuff, and a selection is commercially available for longer-term use. They are larger bore catheters and usually require flushing with stronger solutions of heparin to maintain paten-cy (e.g. 5000 U/ml of heparin). The volume of heparin flush used should be equal to the volume of each lumen to avoid systemic heparinization of the patient.

It should be noted that for optimum flow rates, it may be necessary to position the tip of the catheter at the junction of the right atrium and superior vena cava (SVC; Vesely, 2003) to avoid irritation/thrombus formation when the catheter tip abuts onto the vein wall (Fletcher & Bodenham, 2000).

PICC

Peripherally inserted central catheters represent a vascular access device (VAD) that can be considered to have an intermediate role in central venous access. These catheters are usually inserted at the bedside via an antecubital vein and are available with single or multiple lumina. In the haematology setting, they are well suited for ambulatory or outpatient therapy (Whitman, 1996) as opposed to intensive inpatient therapy but have been shown to be associated with a higher incidence of thombosis in patients with haematological malignancies (Cortelezzi *et al.*, 2005). This is an important consideration in patients who have had previous thromboses, and in those who are receiving therapy which may increase the thrombotic tendency like thalidomide. Peripherally inserted central catheters can be made of either silicon rubber or polyurethane, the former being associated with a lower risk of thrombosis (Galloway & Bodenham, 2004). However, polyurethane PICC are recommended because polyurethane is a tougher material, enabling thinner lumen walls and larger internal diameters of the lumina. This significantly increases flow rates and reduces the potential for breakage and rupture of the catheter (Hadaway, 1995; Mayer & Wong, 2002). This is an advantage because of the volume of blood and platelet infusions required by haematology patients.

The various types of catheter available are summarized in Table 1. An experienced member of the haemato-oncology team should make the decision regarding which type of catheter is most appropriate at the outset of therapy, to avoid multiple catheterizations. The decision should be made based on diagnosis, length and type of therapy, patient preference, clinical status, availability of patent veins, operator experience and previous central venous access history (Hamilton & Fermo, 1998; Hamilton, 2000; Chernecky

Table 1. Types of commercially available catheter		
Catheter type	Advantages	Disadvantages
Nontunnelled catheters	Choice of sites Easy to insert and remove Multiple lumina available	Short-term use
Skin-tunnelled catheters*	Lower infection rates than nontunnelled Long-term use	More complex insertion and removal
Ports	No external catheter Cosmetically attractive Patient can swim/bathe as normal Low maintenance Long-term use Lower infection rates than skin-tunnelled catheters	Surgical insertion and removal Less suitable for frequent repeated access
Apheresis/dialysis catheters Nontunnelled (e.g. Vascath™ Kimal) Skin-tunnelled	Permit high blood flow rates Easier to insert and remove Lower infection rates than nontunnelled devices Long-term use Good for patients with poor peripheral access who require both PBSC harvest and transplant procedure	Large bore Require flushing with concentrated heparin (for example 5000 U/ml, according to manufacturer guidelines) solution to maintain patency. Flush solution must be withdrawn prior to use Short-term use Complex insertion and removal Best inserted via internal jugular or femoral routes
PICC	Easy to insert and remove Do not require platelet support or correction of clotting prior to insertion/removal	Higher thrombosis rate particularly with polyurethane variety. Polyurethane variety required to infuse blood/platelets because has greater internal diameter than silicone variety Slower flow rates particularly in silicone/valved varieties Catheter longevity lower than with skin-tunnelled devices Incidence of malposition greater than in other types of CVC

*Valved skin-tunnelled catheters are not suitable for apheresis, whereas occasionally the other types of skin-tunnelled catheters can be used for returning blood during an apheresis procedure.

et al., 2002). For example, if an allogeneic transplant is planned, a double or triple lumen skin-tunnelled catheter should be inserted at the outset to ensure adequate access throughout chemotherapy and the subsequent transplant.

Patient care prior to catheter insertion

The procedure, including risks and benefits, should be explained to the patient. The 'operator' should under-take a physical assessment, vein assessment and history of previous central venous catheterizations. Small, portable ultrasound imaging devices provide quick confirmation of vein patency. The presence of venous collaterals on the chest wall/abdomen may signify deep venous obstruction. A history, or signs of SVC obstruction is highly significant, as is a history of difficulties or failure of insertion by a competent operator using X-ray screening or ultrasound. If there is a history of a prior thrombus it is prudent to perform

formal ultrasound imaging studies with Doppler measurements, on both the affected and unaffected side, to exclude thrombus and ensure vein patency. Ultrasound gives useful information at most sites but cannot image the SVC. Other modalities including conventional venography, CT with contrast, MRI venography and transoesophageal ultrasound all have advantages. Difficult, or potentially difficult cases should be discussed with a vascular radiologist. Stenting techniques can be used to restore patency to stenosed veins.

It is generally accepted that the platelet count should be $>50 \times 10^9$/l prior to insertion of a catheter other than a PICC (BCSH, 2003), and the INR <1.5. (Ansell *et al.*, 2004; Douketis, Johnson & Turpie, 2004) Problems may arise when patients are refractory to platelets, have idiopathic thrombocytopenic purpura (ITP) or thrombotic thrombocytopenic purpura (TTP), or in the presence of deranged clotting, for example, in acute promyelocytic leukaemia. The risks and benefits of insertion in terms of type and site of catheter must be assessed on an individual basis. Where the risk of bleeding is increased, or when difficulties with insertion are anticipated, use of experienced personnel and ultrasound guidance are essential (Hatfield & Bodenham, 1999) to maximize the likelihood of an atraumatic, 'first pass' procedure. Additionally, use of lidocaine with adrenaline 1 : 200 000 as local anaesthetic will reduce subcutaneous bruising/bleeding. The increasing recognition of the risks associated with the use of blood products mandates assessment of need on an individual basis rather than routine correction of all minor abnormalities of platelet count and coagulation studies.

Antibiotic prophylaxis

In a meta-analysis of published research, the Center for Disease Control in the United States of America (O'Grady *et al.*, 2002) identified that the use of antimicrobial prophylaxis routinely before insertion or during use of an intravascular catheter does not prevent catheter colonization or BSI (evidence level 1A; i.e. strongly supported by well-designed experimental, clinical, or epidemiologic studies). The Department of Health (Pratt *et al.*, 2001) has issued guidelines limiting the use of vancomycin. They state that the agent should not be used in the following circumstances.

- As treatment in response to a single blood culture positive for coagulase-negative staphylococcus, if other blood cultures drawn in the same time frame are negative.
- For routine prophylaxis.
- When there is a catheter-related infection involving beta-lactam-sensitive organisms.
- As continued empiric therapy for presumed infections in patients whose cultures are negative for beta-lactam-resistant gram-positive organisms.

Antibiotic cover may be appropriate if simultaneous insertion and removal procedures have to be performed in a known case of catheter-related sepsis. However, it is not routinely recommended.

Catheter insertion

As previously mentioned, it is essential that only experienced personnel insert central venous catheters, to minimize infection and other complications, particularly in the presence of low platelets, deranged clotting and/or in the critically ill patient. This includes the short-term multiple lumina nontunnelled catheter, which is often inserted by junior medical personnel who have undergone minimal training with little clinical supervision in insertion techniques.

Where possible, the procedure should be performed in a clean area designated for CVC insertion such as the X-ray department, operating theatre, or a procedure suite where a high standard of asepsis is practiced. Units which currently insert tunnelled CVCs on the wards should audit their procedural complications and infection rates in order to support or refute continuation of this practice. Whatever the environment, maximum sterile barrier conditions (mask, cap, sterile gloves, gown and large drape) have been shown to lower the risk of acquiring catheter-related infections (Mermel *et al.*, 1991; Raad *et al.*, 1994; O'Grady *et al.*, 2002). Published evidence shows, however, that the risk of infection depends mainly on the presence of bacteria on the skin (Fletcher, 2005). Hence, skin cleansing is the most important part of care before catheter insertion. Two per cent aqueous chlorhexidine has been shown to be superior to either povidone-iodine solution or 70% alcohol in reducing catheter-related blood stream infections (Maki, Ringer & Alvarado, 1991). More recently, 2% chlorhexidine

in alcohol has been recommended (Pratt *et al.*, 2001; Pellowe *et al.*, 2003) and this should be used for skin antisepsis prior to catheter insertion and for insertion site dressing changes.

Anatomical surface markings can be unreliable for the initial puncture and ultrasound guided insertion of catheters (excluding PICC) is strongly recommended, whenever possible, by operators experienced in the use of ultrasound techniques (NICE, 2002; Hind *et al.*, 2003). Ultrasound can be used for PICC insertion but is not usually necessary. It may, however, be useful to check vein patency, for proximal approaches or when the peripheral veins are not palpable because they lie deep within the subcutaneous tissue. The use of ultrasound ensures patency of the vein and has been shown to reduce insertion-related complications (NICE, 2002; Hind *et al.*, 2003). An image intensifier can be used to image the target vein with contrast and to check correct positioning of the guidewire and catheter tip. Its use is recommended when inserting tunnelled catheters and ports. Catheters are normally inserted under local anaesthesia with, or without sedation such as intravenous midazolam or other combinations of sedative drugs, according to local policy. Occasional patients with severe needle phobia or who become dyspnoeic when lying flat/head down will require a general anaesthetic. The majority of procedures should be performed by Seldinger wire techniques, reserving open surgery for difficult cases or small children. Specialist vascular radiology input will be required for the more difficult cases needing vein stenting or unusual routes of access.

No randomized controlled trials have satisfactorily compared infection or thrombosis rates for catheters placed via the jugular, subclavian and femoral sites (Pellowe *et al* 2004), although in nonrandomized comparisons, infection rates are higher with femoral catheters (Goetz *et al.*, 1998) [See below]. In adults, the subclavain approach may have an advantage because there is some evidence to suggest that it has lower infection rates than the internal jugular approach (Mermel *et al.*, 1991; Richet *et al.*, 1991), but this must be balanced against the risks of mechanical complications. For example, catheters placed via a subclavian approach are more likely to cause thrombosis than those placed via the internal jugular route (Trerotola, 2000), and are therefore more likely to

cause secondary stenosis (Knutstad, Hager & Hauser, 2003).

A lateral approach when using the subclavian vein avoids 'pinch off' of the catheter, which is a rare complication referring to entrapment of the catheter between the clavicle and the first rib (Polderman & Girbes, 2002). Ultrasound-guided insertions in the subclavian area will tend to move the puncture site laterally because of the presence of the probe and clavicle (Sharma, Bodenham & Mallick, 2004). An alternative is to use the internal jugular vein, which is particularly useful in patients with abnormal coagulation, as it reduces the risk of inadvertent arterial puncture (Lameris *et al.*, 1990), although tunnelling can be more difficult. Debate continues based on retrospective audits concerning the relative merits of right or left insertion sites and the perceived differences in rates of thrombosis, infections and mechanical problems. Other considerations such as cosmetic appearance may be important to patients and care should be taken to avoid lumpy tunnelling in the neck and to arrange for the external portion of the line to be concealed under clothing.

In patients in whom the internal jugular and both subclavian veins are occluded or otherwise unavailable for puncture, or in the event of SVC obstruction, catheters may be inserted into the femoral vein, although infection rates are higher with this approach (Goetz *et al.*, 1998; O'Grady *et al.*, 2002), as are rates of deep vein thrombosis (Trottier *et al.*, 1995; Joynt *et al.*, 2000). Tunnelling can take the exit site out of the groin onto the relatively clean anterior abdominal wall. The femoral approach may also be useful in emergency situations or in the presence of severe thrombocytopenia and/or coagulopathy, where it is easier to apply pressure or achieve haemostasis in the event of bleeding. The straight course of the vein makes it ideal for stiff dialysis-type catheters, which do not traverse tight angles easily.

With subcutaneous ports, subclavian or internal jugular venous access is achieved using aseptic conditions, in the same way as for skin-tunnelled catheters. If patients are accessing their own port, then it should be located low on the rib cage or upper arm, for easy access. When patients are not accessing their own port, then the port is usually located on the upper rib cage near the clavicle. Ports near the sternum provide better needle stability and ease of access. Adequate

subcutaneous tissue will prevent erosion through the skin. If the port is placed too deeply or there is excess adipose tissue, it can make access difficult. Placement under the arm, in the breast or the soft tissue of the abdomen should be avoided (Goodman, 2000). There are both low and high profile ports available.

Immediate patient care after catheter insertion

Tip placement should be checked by X-ray prior to use and the position of the catheter tip documented in the patient file. Optimum tip position is the distal superior vena cava or the upper right atrium (Fletcher & Bodenham, 2000).The carina can be used as an approximate marker of the level of the pericardial reflection. Catheters inserted from the left side tend to need the tip to lie at the junction of the SVC and RA or within the upper RA, in order for the catheter tip to lie within the long axis of the vessel. Changes in tip position on standing may be significant. Chest X-rays taken within 1–2 h of placement may not demonstrate a slowly developing pneumothorax or bleed. A further chest X-ray is required if the patient becomes dyspnoeic or complains of laterat chest wall discomfort/pain. Pneumothorax usually relates to sub-clavian vein catheterization but can also result from attempted internal jugular cannulation. Many pneumothoraces do not require drainage but should be monitored by serial X-rays. Smaller bore Seldinger-type drains are suitable for draining slowly accumulating collections when treatment is required, and large bore traditional chest drains are rarely required.

A transparent semi-occlusive dressing such as Op-Site 1 V 3000™ is recommended (Reynolds, Tebbs & Elliott, 1997; Treston-Aurand *et al.*, 1997). Transparent dressings reliably secure the device, permit continuous visual inspection of the catheter site, permit patients to bathe and shower without saturating the dressing, and require less frequent changes than do standard gauze and tape dressings. The dressing should be changed after the procedure if bleeding has occurred, but otherwise not until 24 h postoperatively. It should then be changed weekly if there are no signs of bleeding and/or infection. However, a recent review has found no consistent benefit for any type of dressing (Gillies *et al.*, 2003). A meta-analysis has assessed studies that compared the risk for catheter-related BSIs for groups using transparent dressings *vs.*

groups using gauze dressing. The risk for CRBSIs did not differ between the groups. The choice of dressing can be a matter of preference. If blood is oozing from the catheter insertion site, gauze dressing might be preferred (O'Grady *et al.*, 2002).

For patients with a tunnelled catheter, the upper suture over the insertion site into the vein should be removed at 7–10 days and the lower one at the exit point should be removed after 3 weeks. Recent evidence supports the use of securing devices, including tapes, adhesives or staples (Motonaga, Lee & Kirsch, 2004), particularly with nontunnelled CVCs and PICC. These obviate the need for sutures at the exit site or around the vein, which can cause difficulties with subsequent line removal. Securing devices have also been shown to reduce infection rates when compared with sutures (Crnich & Maki, 2002; Yamamoto *et al.*, 2002; Frey & Schears, 2006). Sutures over an implanted port insertion site are removed after 7–10 days, although some operators may use dissolvable sutures to close the wound. Peripherally inserted central catheters and nontunnelled catheters should always be covered with a dressing, although skin-tunnelled catheters may not require a dressing once the wound has healed (Morris *et al.*, 1995; O'Grady *et al.*, 2002). This can be reviewed on an individual basis. Implanted ports do not require any dressing once the wound has healed.

Long-term catheter care

For skin-tunnelled devices, it is advisable to either secure the ends to the chest wall with tape or to use a 'neck-bag' to take the weight of the free ends. Showering is preferable to bathing, and swimming must be avoided with any external catheter, in order to prevent colonization by Gram-negative organisms, especially *Pseudomonas* spp.

Flushing with the correct solution and technique is essential to maintain catheter patency, and only single-dose solutions should be used. The use of heparin flushes *vs.* normal saline intermittent flushes remains controversial. Many clinicians still recommend the use of heparin (10 U/ml) to prevent thrombus formation and ensure catheter patency, but the efficacy of this is unproven (Pellowe *et al.* 2004). Exposure to heparin should be minimized to prevent the development of heparin-induced thrombocytopenia (HITS) and to

avoid development of bleeding complications because of inadvertent heparinization secondary to multiple heparin flushes (Passannante & Macik, 1998). A review of the current evidence concluded that heparin doses of 10 U/ml are no more beneficial than flushing with normal saline alone (Pellowe *et al.* 2004). However, there are exceptions. For example, apheresis/dialysis catheters require heparin flushes to maintain patency, and some manufacturers and clinicians recommend heparin flushes, particularly when catheters are infrequently accessed. The need for heparin may be a function of bore, as larger bore catheters allow quicker back-tracking of blood up the lumen. Because thrombi and fibrin deposits on catheters might serve as a nidus for microbial colonization of intravascular catheters, the use of anticoagulants might have a role in the prevention of CRBSI. Because the majority of heparin solutions contain preservatives with antimicrobial activity, whether any decrease in the rate of CRBSI is a result of the reduced thrombus formation, the preservative, or both is unclear (O'Grady *et al* 2002).

Flushing protocols for the main types of catheter are shown in Table 2 although the manufacturers' recommendations should always be followed. Syringe size can be important as the smaller syringes create greater pressure and may contribute to catheter rupture if excessive pressure is exerted (Conn, 1993; Primhak, 1998). Care must always be taken to maintain patency by using a pulsatile flush method and by maintaining positive pressure while removing the syringe at the end of flushing in order to avoid reflux of blood (Goodwin & Carlson, 1993; Dougherty, 2004). The use of needle-free connectors is recommended as these have been shown to reduce infection (Yebenes *et al.*, 2004). Patients should be educated in the care of their catheters, and a recent randomized study has shown a reduction in catheter-related infections when patients are made responsible for care of the catheter (Moller *et al.*, 2005).

Several prospective and randomized studies have shown that specialist teams can reduce infection rates (Miller *et al.*, 1996; Fitzsimmons *et al.*, 1997; Meier *et al.*, 1998; Soifer *et al.*, 1998; Solomon & Stoddard, 2001; Hamilton, 2004), and where possible the use of these should be developed. Infections can be minimized by careful hand washing and catheter site care. The external surfaces of the access port should be

Table 2. Catheter flushing protocols

Catheter type	Solution	Frequency	Cautions
Nontunnelled	10 ml saline 0.9% ± 5 ml heparinized saline solution (10 U/ml)	After each access when used intermittently, or weekly	
Skin-tunnelled*	10 ml saline 0.9% ± 5 ml heparinized saline solution (10 U/ml)	After each access or weekly	
Ports*	10 ml saline 0.9% ± 5 ml heparinized saline solution (10 U/ml)	After each access or monthly	Do not use a syringe smaller than 10 ml in size, to avoid catheter rupture
Apheresis/dialysis	10 ml saline 0.9% plus 1000 U/ml or 5000 U/ml Catheter volume only	After each access or weekly	Calculate 'dead space volume' to avoid systemic heparinization – usually printed on the CVC lumen
PICC*	10 ml saline 0.9% ± 5 ml heparinized saline solution (10 U/ml)	After each access, or at least weekly	

*Valved varieties require 10 ml saline 0.9% solution to flush. No heparin required. Refer to manufacturer guidelines in each case.

disinfected with a chlorhexidine gluconate solution unless contraindicated by the manufacturers instructions (Pellowe *et al.* 2004; Pratt *et al.*, 2001). Either a sterile (sterile gloves) or 'nontouch' (clean gloves) technique must be utilized when accessing any CVC lumen. A blood sampling protocol should be developed locally, but must include instruction on the removal of the heparinized dead space (approximately 5 ml) prior to sampling, to avoid erroneous results. The volume to be removed before coagulation studies are performed is uncertain with central venous catheters, but for APTT studies from arterial cannulae it is recommended that six times the dead space volume is removed (Laxson & Titler, 1994). Coagulation studies in such circumstances may produce erroneous results, particularly with apheresis or dialysis catheters where stronger heparin solutions have been used, and, if there is any doubt, the sample should be taken from a peripheral vein. In the bone marrow transplant setting, a lumen for taking blood for ciclosporin and other drug levels should be identified and the drugs administered through a different lumen.

Patient information

A patient's guide should include the following sections: (i) What constitutes a central venous access device. (ii) The advantages and disadvantages of having a central venous access device. (iii) Any risks involved in the insertion of a central venous access device. (iv) Care of the device. (v) Removal of the device.

Locally generated patient information leaflets are recommended but should not be a substitute for careful and detailed explanation by a nurse/doctor experienced in the care of central venous catheters. Generally speaking, the following information must be provided, with a 24-h cover arrangement:

- How to contact a nurse or doctor if the exit site is red, sore, oozing pus or in the event of a fever of >38 °C.
- How to contact a nurse or doctor if the catheter becomes damaged or leaks.
- How to contact a nurse or doctor if the arm becomes swollen or if any distended veins become apparent on the chest or neck.
- How to contact a nurse or doctor if breathless or pain are experienced.

Management of problem patients

- If the patient is *thrombocytopenic* and there is evidence of bleeding after catheter insertion, then the patient should receive further platelet transfusion(s) to maintain the count in excess of $50 \times 10^9/l$ until bleeding stops, bearing in mind problems may exist in patients refractory to random donor platelets or in those suffering from ITP or TTP (BCSH, 2003). In these situations the application of pressure dressings and topical tranexamic acid may help. Prolonged compression (15 min plus) will often stop bleeding. It should not be overlooked, however, that there are no published prospective, randomized studies to support or negate the theory that the level of platelet count at time of CVC insertion should be maintained above $50 \times 10^9/l$ to reduce potential for significant bleeding problems. Barrera *et al.* (1996) concluded that thrombocytopenia is not the only risk factor for bleeding and concludes that other variables such as insertion site, number of needle passes to cannulate the vein, and expertise are more pertinent. Similarly, the study by Ray and Shenoy (1997) concluded that peri-procedural platelet transfusions have little effect on bleeding outcome. Other studies in patients with liver disease and complex haemostatic defects have found that a platelet count of $<50 \times 10^9/l$ was an independent risk factor for bleeding in comparison with raised INR or prolonged PT (Doerfler, Kaufman & Goldenberg, 1996; Fisher & Mutimer, 1999; Mumtaz *et al.*, 2000). Robust, randomized studies are necessary to achieve evidence-base guidance in these complex situations.

- In patients with *disseminated intravascular coagulation*, for example, in association with acute promyelocytic leukaemia, there should be vigorous correction of any abnormality of coagulation. The prothrombin time should be <1.5 times normal and fibrinogen >1.0 g/l. Patients taking oral anticoagulants should stop their tablets to achieve an INR <1.5 before catheter insertion. If time is limited, factor concentrates, fresh frozen plasma (FFP), or vitamin K may be required, but the latter, in high doses, may interfere with subsequent anticoagulation (Baglin, Keeling & Watson, 2005). Reversal of therapeutic anticoagulation with vitamin K is usually achieved within 4–6 h of intravenous administration of vita-

min K, and within 24 h of oral administration (Watson *et al.*, 2001). Phytomenadione (Konakion®) doses of up to 2 mg intravenously, or 5 mg orally are recommended. Complete and rapid reversal of over anticoagulation is more readily achieved with a factor concentrate rather than with FFP (Makris *et al.*, 1997; Evans, Luddington & Baglin, 2001). Intravenous vitamin K should be given if reversal is to be sustained (Yasaka *et al.*, 2002), and repeat administration may be required after 24 h.

Intravenous unfractionated heparin (UFH) should be stopped 3 h before catheter insertion and restarted when haemostasis is secured. In patients receiving prophylactic subcutaneous low molecular weight heparin (LMWH), catheter insertion can be undertaken 12 h after the last injection; for patients receiving therapeutic subcutaneous LMWH, the time to catheter insertion should be extended to 18 h after the last injection. Heparin can be recommenced once the operator has confirmed haemostasis is secure, usually within 2 h of catheter insertion. Substitution with intravenously infused UFH or insertion of an IVC filter should be considered if there is a very high thrombotic risk. Expert haematology advice should be sought.

- *Haemophiliac* patients (with haemophilia A, B or C) will require appropriate factor replacement, as may patients with other inherited coagulopathies. Correction should be maintained for >48 h. Clinicians caring for such patients should seek advice from their local haemophilia reference centre.
- *Infection* at the time of catheter insertion represents a relative contra-indication to proceeding, and consideration should be given to temporary, nontunnelled catheter placement or temporary use of peripheral cannulae, but the risks and benefits should be considered for each patient on an individual basis. If the patient has a unilateral skin infection on the anterior upper chest wall, the unaffected side should be used for catheter placement. Targeted antibiotic prophylaxis may be warranted in these cases.

Routine replacement of nontunnelled CVCs should not be used as a method for preventing catheter-related infection, as this has not been shown to reduce infection rates (Cook *et al.*, 1997; O'Grady *et al.*,

2002). Guidewire-assisted catheter exchange to replace a malfunctioning catheter is acceptable if there is no evidence of infection. However, if infection is suspected, the existing catheter should be removed and a new catheter inserted at a different site (Pratt *et al.*, 2001). This technique is generally impractical for cuffed tunnelled catheters or ports, when it may be technically easier and safer to insert a new catheter into a clean site.

- A patient who has received previous *radiotherapy* to one side of the chest should have the catheter inserted on the opposite side. Patients who have undergone mastectomy and lymph node dissection should have the catheter placed on the opposite side. Catheters can be tunnelled onto the arm or other sites if the chest wall is unsuitable. Catheters should be kept away from breast prostheses and pacemaker boxes/wires.

Prevention and management of catheter complications

The main complications are: (i) catheter-related infection; (ii) catheter malfunction; and (iii) catheter-related thrombosis.

Catheter-related infection

Infection rates vary from 0.08 per 1000 days in oncology outpatients to 19/1000 catheter days in the critically ill (Fletcher, 2005). Haemato-oncology infection rates probably lie somewhere within this range but catheter-related blood stream infections can be severe and life-threatening depending on the micro-organism involved. The Department of Health (Pratt *et al.*, 2001) has made recommendations for good practice regarding prevention, diagnosis and treatment of infections (and other aspects of central venous catheterization), which have recently been updated by Pellowe *et al.* (2004). There are three categories:

- A *catheter-related blood stream infection* is defined as at least two blood cultures positive with the same organism, obtained from at least two separate sites at different times, in association with evidence of colonization of the catheter with the same

Table 3. Recommendations for the management of catheter related infections		
Category of infection	Non-neutropenic patient	Neutropenic patient
Exit site infection	Remove catheter if no longer needed Treat empirically with *flucloxacillin	Remove catheter if no longer needed Initial empirical therapy including glycopeptide Treat for 10–14 days or longer until infection resolved Modify according to isolates Remove catheter if evidence of progression or if blood cultures are positive for *Staph. aureus*, *Pseudomonas* spp., *Mycobacterium* spp., or fungi
Tunnel infection	Remove catheter if no longer needed Treat empirically with *flucloxacillin	Remove catheter if no longer needed Initial empirical therapy including glycopeptide Treat for 10–14 days or longer until resolution of soft tissue infection. Modify according to isolates If tracking continues to spread remove catheter
Presumed catheter-related bloodstream infection	Remove catheter if no longer needed Treat empirically with antibiotics targeted against isolates	Remove catheter if no longer needed Initial empirical antibiotic therapy. Modify according to isolates. Treat for at least 10–14 days Remove catheter if cultures remain positive after 48 h of therapy or if proven catheter-related infection with *Staph. aureus*, *Pseudomonas* spp., *Mycobacterium* spp., or fungi

*Unless known to be colonized with MRSA, when a glycopeptide should be used

organism. The latter part of the definition can only be strictly fulfilled by removing the catheter.

- An *exit site infection* presents with erythema, tenderness and occasionally a discharge at the insertion site.
- A *tunnel infection* is characterized by pain and induration along the track of the catheter.

The incidence of these infections varies in different centres with different groups of patients and different practices.

The management of catheter infections remains controversial. Attempts should be made to make a microbiological diagnosis by culturing blood from all catheter lumina, a peripheral sample of blood and the exit site before commencing antibiotics. However, in clinical practice, it is usual for broad-spectrum antibiotics to be initiated while awaiting culture results.

Table 3 summarizes current recommendations based upon consensus and the literature, although the decision to salvage or remove a catheter should be made following discussion with the microbiologist and after consideration of the patient's clinical status and his position on the treatment pathway. Recent evidence suggests that *in situ* use of glycopeptides may be effective for coagulase negative staphylococcal infections (Ley *et al.*, 1996; Giacometti *et al.*, 2005). The 'antibiotic lock' technique may also be effective in reducing catheter-related bacteraemia (Carratala, 2002; Garland *et al.*, 2005; Rijnders *et al.*, 2005; Fernandez-Hidalgo *et al.*, 2006; Kim *et al.*, 2006). Certain organisms carry a much greater risk of treatment failure and disseminated infection (see Table 3). A catheter lock solution containing citrate and taurolidine (TauroLock™) has been used particularly in the

setting of haemodialysis catheters (Allon, 2003; Betjes & van Agteren, 2004), and is designed to render the internal flow passages resistant to clot formation and hostile to bacterial and fungal growth. This may also prove useful in the haemato-oncology setting, but requires further evaluation.

It is recommended that administration sets are changed every 72 h when used for continuous infusions of solutions, but these should be changed more frequently if used for intermittent therapies, blood, or lipids (NICE, 2003; RCN, 2005). Needle-free connectors must be changed in accordance with manufacturer's recommendations (Medicines and Healthcare Products Regulatory Agency (MHRA), 2005).

Catheter malfunction

Partial and complete catheter blockage is evidenced by difficulty in aspirating blood or infusing fluid. Forcible introduction of fluid down an obstructed lumen may cause catheter rupture. Catheter occlusion may include blockage resulting from kinking of the catheter, 'pinch off syndrome', occlusion of the catheter tip on the vessel wall, fibrin sheath or fibrin flap or luminal thrombus, or migration of the tip into a smaller vessel. Plain X-ray or a catheter contrast study may be helpful in confirming the diagnosis. Initially, fibrin sheaths manifest with catheter dysfunction, progressing to complete failure. They are usually discovered 1–2 weeks after placement (Crain, Horton & Mewissen, 1998). Infusion substances can penetrate between the catheter wall and the fibrin sheath in a retrograde manner, along the catheter to the site of venous insertion, and even out to perivascular and subcutaneous layers. This can lead to cutaneous or subcutaneous necrosis. Untreated fibrin sheaths are associated with increased risk of complications, but interventional radiologists may be able to temporarily salvage catheter function by using percutaneous, intravascular fibrin sheath stripping via a transfemoral approach (Knutstad, Hager & Hauser, 2003).

Where catheter occlusion is due to thrombus without symptomatic thrombosis, instillation of Hepsal (heparin sodium 10 U/ml) may be effective. If not, urokinase 10 000 U/ml reconstituted in 4 ml normal saline may be tried, using 2 ml of solution into each catheter lumen and ensuring that intraluminal volumes only are instilled. Urokinase is manufactured by Medac and is available on a named patient basis. The solution should be injected gently into the catheter with a push-pull action to maximize mixing within the lumen. The lumen should then be clamped and left for at least 2–3 h. The catheter should then be unclamped and the solution containing disaggregated clot aspirated (Gabriel, 1999; Dougherty, 2004). It has not been shown to be cost-effective or clinically necessary to leave the solution in the lumen for longer periods, such as between episodes of haemodialysis.

Very recently, an alternative urokinase preparation called Syner-KINASE has become available. This is manufactured by Syner-med and has been licensed in the UK for clearing blocked intravenous catheters. It is highly purified, extracted from human urine, and tested by PCR to exclude viral contamination. This is said to be free of the technical problems associated with manufacture, which occurred with the previous brands of urokinase.

An alternative to urokinase is Cathflo Activase (Alteplase), which is a recombinant human tissue plasminogen activator (t-PA; Deicher *et al.*, 2002). Again, this is available on a named patient basis and is manufactured by Genentech.

Other reasons for catheter malfunction can include damage to the catheter. For example, 'pinch off' as described earlier, or kinking of the catheter. Occasionally, the tip of the catheter can migrate, particularly if the catheter is short and the tip initially lies in the upper superior vena cava or brachiocephalic vein. This may result in the catheter ceasing to function. Repeat chest X-rays may help in diagnosing these problems. Internal repair of a damaged catheter is no longer recommended because of risk of infection and/or air embolus. External repairs of damaged catheters can be performed using kits provided by the manufacturers.

Catheter-related thrombosis

Catheter-associated thrombosis may be spontaneous, or may result from a prothrombotic state associated either with underlying malignancy or treatment, particularly with L-asparaginase, thalidomide or lenalidamide. The catheter will normally require removal if thrombosis is confirmed. Intraluminal thrombosis may be prevented by adhering to appropriate flushing protocols and ensuring good placement of the catheter

tip (Table 2). The use of low dose warfarin is now contraindicated as it has been shown to be of no apparent benefit for the prophylaxis of symptomatic catheter-related thrombosis in patients with cancer (Couban *et al.*, 2005; Young *et al.*, 2005). Dose-adjusted warfarin may be superior but at the cost of an increased risk of bleeding. There are no published data concerning ideal levels of anticoagulation in thrombocytopenic patients or on the recommended duration of anticoagulant therapy in catheter-related thrombosis. If the catheter is removed because of confirmed thrombosis, therapeutic doses of low molecular weight heparin and warfarin should be given in nonthrombocytopenic patients. In thrombocytopenic patients low molecular weight heparin may be used, adjusting the dose in accordance with the level of thrombocytopenia. Full doses can be given if the platelet count exceeds 80×10^9/l (BCSH, 2006), in the absence of bleeding and where renal function is normal. With platelet counts below this, the decision regarding heparin dose should be based on clinical need, the presence or absence of bleeding, and whether or not the platelet count increments with platelet transfusion. Renal function should be regularly monitored during treatment.

Anticoagulation should be continued for a period of approximately 3 months in uncomplicated cases, with a target INR of 2.5 (range: 2.0–3.0) when warfarin is being used. If there is clinical or radiological evidence of persistent thrombus, anticoagulation should be continued for a longer period. Mechanical clot lysis or local application of thrombolytic drugs to rapidly restore vein patency can be effective if the vein is occluded with fresh thrombus. Collaboration with vascular surgical or interventional radiology teams is advised.

If the patient has a PICC, any swelling of the arm should be monitored. Swelling alone does not confirm thrombosis, and if suspected it must be confirmed radiologically, by Doppler ultrasound, CT scanning or other imaging. If confirmed, the PICC should be removed and anticoagulants commenced as described previously.

Technique of catheter removal

Indications for catheter removal include: (i) catheter-related infection, (ii) persistent catheter occlusion, (iii) catheter-related thrombus, (iv) damaged catheter, and (v) the end of treatment. Removal of a skin-tunnelled catheter requires local anaesthetic and minor surgical cut-down to remove the cuff if the catheter has been *in situ* for more than approximately 3 weeks. The patient should lie down to avoid air embolus. Simple traction can remove the catheter and cuff in catheters, which have been in less than three weeks. Gentle traction can be attempted, but if difficulty is encountered it is important to stop prior to the catheter breaking. Removal should be undertaken by experienced personnel. The platelet count should be $>50 \times 10^9$/l and the INR less than 1.5. Ideally, 12 h should have elapsed after prophylactic low molecular weight heparin, and 18 h after a therapeutic dose. The skin-tunnelled catheter can be removed under local anaesthetic. Use of a local anaesthetic agent containing epinephrine (w/v/1 : 200 000) may be helpful in the presence of thrombocytopenia and deranged clotting, to minimize local bleeding. A small incision (2 cm should be adequate) is made alongside the cuff and blunt dissection used to free the cuff and avoid catheter damage prior to removal. If the cuff is at the exit site it can be removed by enlarging the exit site wound. The intravascular portion should be removed safely prior to cutting the catheter (Galloway & Bodenham, 2004). If the catheter tip is sheared off during removal, it is likely to embolize into the right heart or pulmonary artery and will require urgent retrieval by vascular radiologists using a snare, under fluoroscopic guidance (Bessoud *et al.*, 2003). Internal repair of a damaged catheter is no longer recommended because of risk of infection and/or air embolus. External repairs to damaged catheters can be performed using kits provided by the manufacturers.

It is important to remove the catheter in the direction of the tunnel. The catheter should be inspected carefully after removal to ensure that it is complete, and, if infection is suspected, the tip should be sent to the microbiology department for culture. The cut-down site should be sutured with a fine 3/0 or 4/0 monofilament suture. Large incisions and thick sutures should be avoided as these scar badly. After removal, pressure should be applied to the exit point, tunnel and venotomy site and an occlusive dressing placed over the exit site to avoid air embolism. Ports require surgical removal in theatre or equivalent. Peripherally inserted central catheters and short term,

nontunnelled catheters can be removed at the patients bedside and pressure applied. The tips should be sent for microscopy and culture if clinically indicated.

Recommendations for audit

A locally based audit should include patient identification data, diagnosis, date of catheter insertion, number of previous catheters, operator and department where the catheter was inserted, complications associated with the catheter, date of and reason for removal. Each unit should monitor their infection rates/1000 catheter days to observe any changes or trends in infection rates and be mindful of the emergence of resistant bacteria.

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DISCLAIMER

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