Access technique and its problems in parenteral nutrition – Guidelines on Parenteral Nutrition, Chapter 9

Technik und Probleme der Zugänge in der parenteralen Ernährung – Leitlinie Parenterale Ernährung, Kapitel 9

Abstract

Catheter type, access technique, and the catheter position should be selected considering to the anticipated duration of PN aiming at the lowest complication risks (infectious and non-infectious). Long-term (>7–10 days) parenteral nutrition (PN) requires central venous access whereas for PN <3 weeks percutaneously inserted catheters and for PN >3 weeks subcutaneous tunnelled catheters or port systems are appropriate. CVC (central venous catheter) should be flushed with isotonic NaCl solution before and after PN application and during CVC occlusions. Strict indications are required for central venous access placement and the catheter should be removed as soon as possible if not required any more. Blood samples should not to be taken from the CVC. If catheter infection is suspected, peripheral blood-culture samples and culture samples from each catheter lumen should be taken simultaneously. Removal of the CVC should be carried out immediately if there are pronounced signs of local infection at the insertion site and/or clinical suspicion of catheter-induced sepsis. In case PN is indicated for a short period (max. 7–10 days), a peripheral venous access can be used if no hyperosmolar solutions (>800 mosm/L) or solutions with a high titration acidity or alkalinity are used. A peripheral venous catheter (PVC) can remain in situ for as long as it is clinically required unless there are signs of inflammation at the insertion site.

Keywords: intravenous access, central venous catheter, handling of central catheter, catheter-related infections, in-line filter

Zusammenfassung

Abhängig von der voraussichtlichen Dauer der PE sollte der Kathetertyp, die Zugangstechnik und die Katheterposition mit dem geringsten Komplikationsrisiko (infektiös und nicht-infektiös) gewählt werden. Eine langfristige (>7–10 Tage), bedarfsadaptierte parenterale Ernährung (PE) ist auf einen sufficienten zentralvenösen Zugangsweg angewiesen, wobei für eine PE <3 Wochen perkutan eingelegte Katheter und für eine PE >3 Wochen subkutan tunnelierte Katheter oder implantierte Portsyste- nome zur Anwendung kommen. Der zentralvenöse Katheter (ZVK) sollte vor und nach der PE-Applikation und bei ZVK-Okklusion mit physiologi- scher NaCl-Lösung gespült werden. Die Indikationsstellung zur Anlage eines venösen Zugangs muss streng erfolgen und der Katheter sollte schnellst möglich wieder entfernt werden, wenn er nicht mehr benötigt wird. Zur Reduktion des Infekionsrisikos sollten Blutentnahmen aus dem ZVK vermieden werden. Bei Verdacht auf Katheterinfektion sollten gleichzeitig Blutkulturen peripher und aus jedem Katheterlumen entnommen werden. Bei ausgeprägten lokalen Infekthezen der Insertionsstelle und klinischem Verdacht auf Katheter-induzierte Blutstrominfektion ist die ZVK-Neuanlage vorzunehmen. Im Falle einer kurzzeitig indizierten PE (max. 7–10 Tage) kann eine periphere Nephro-Zufuhr durchgeführt werden, wenn keine hyperosmolaren Lösungen (>800 mosm/L) verwendet werden sollen.
Central venous access

- Long-term (>7–10 days) parenteral nutrition (PN) requires central venous access (A).
- Strict indications are required for central venous access placement, and the catheter should be removed as soon as possible (A).
- Catheter type, access technique, and the catheter position should be selected considering to the anticipated duration of PN aiming at the lowest complication risks (infectious and non-infectious) (A).

Commentary

PN solutions are administered either via a central venous catheter or over short term via peripheral venous cannulae, depending on the condition of the patient (type of illness, current state of health etc.), composition of the infused solution, amount of energy to be administered, and duration of PN. Accessibility of the venous system needs to be evaluated considering vascular status, anatomy, and coagulation status. PN associated complications such as infections and mechanical problems result in significantly increased morbidity and mortality [1], [2]. Regular monitoring of metabolic response to PN is also required [3]. Any venous access that is no longer required should be immediately removed [4], [5].

PN is usually administered via a central venous catheter because of the high osmolarity of nutrient admixtures. The objective of a central venous catheter (CVC) is to get access to the vena (V) cava. The tip of the CVCs is often placed in the superior vena cava. Peripheral and central venous access sites are available for this placement. When using central venous access sites, the CVC is inserted directly into a large vein close to the heart. The location of the catheter tip should generally be radiologically documented; ECG-controlled position monitoring is possible.

An alternative to central venous cannulation is a peripherally inserted central catheter (PICC) using an ultrasound-guided cannulation of a peripheral vein in the upper arm [6]. A technically simpler method is the placement of a PICC-line in an elbow vein without ultrasound control, and advancement of this peripheral catheter to the superior vena cava. The advantages of these peripheral access sites are lower rates of acute complications such as pneumothorax, life-threatening bleedings, etc. The disadvantage is that local complications (phlebitis etc.) [7], and late complications, especially thromboses and infections, occur more frequently [8] (see also section on peripheral venous access (below) under peripheral venous PN).

Selection of catheters for central venous access

- Central venous catheters inserted by percutaneous cannulation are favoured for short-term administration of PN (A).

Commentary

The estimated duration of PN is extremely important when selecting the type of catheter. If less than three weeks of PN are anticipated, then percutaneously inserted catheters (e.g. by means of Selding technique) are appropriate [9]. The Seldinger method is favoured as it offers significant advantages when compared to other techniques: lower risk of injury with cannulation, lower risk of air embolism [10], [11] and higher success rate [12].

Infusion pumps

- High-caloric PN should preferably be administered with infusion pumps (C).
- PN should always be administered by an infusion pump in neonatal and paediatric patients (C).

Commentary

The supply rate of infusion solutions can be set, with a high degree of accuracy by using infusion pumps, or by employing the effects of gravity and setting the infusion speed via a drop counter. All-in-one solutions should preferably be administered via an infusion pump. The advantage of such devices is a precise control of the flow rate, which may enhance PN tolerance. The drop speed, when using gravity infusions, cannot be regulated as precisely as with the use of infusion pumps, resulting in potentially excessive infusion rates. The use of infusion pumps is generally recommended for infants and children, to secure a controlled flow rate.

Infectious CVC complications

- CVC cannulation predisposes patients to infectious complications (A).
• Blood samples should not to be taken from the CVC to reduce the risk of infection (B).

**Commentary**

There is close correlation between length of hospital stay (LOS) and risk of infection [13], [14], [15]. Thrombotic complications also depend on LOS [15], [16]. Difficult cannulations, severe infectious underlying illnesses, immune deficiency or cannulations carried out under emergency conditions or by inexperienced doctors, predispose patients to infectious CVC complications in PE [17], [18], [19].

Blood sampling from a CVC increase the risk of catheter-associated infections [20], [21], [22], [23], [24]. Patients with structural heart disease and associated risk factors should receive endocarditis prophylaxis prior to cannulation.

**Used catheter/flush system**

- Subcutaneous tunnelled catheters or port systems should be implanted and used for long-term PN, especially for home PN (A).
- Port needles should be replaced every third to seven days (B).
- Routine flushing of non-utilised CVCs or port systems with heparin is not recommended (A).
- CVC should be flushed with isotonic NaCl solution before and after PN application (A).

**Commentary**

Tunnelled or implanted permanent devices (Broviac® or Hickman®/Groshong catheters, port systems) are suitable for long-term PN (>3 weeks) [1]. Broviac® and Hickman®/Groshong catheters are implantable, percutaneously inserted venous silicone catheters. The majority of tunnelled devices have a short polyester cuff attached to the catheter that encourages fibrosis, and therefore anchorage within the subcutaneous tissues, and thus can prevent bacteria from penetrating [25].

If the CVC is temporarily not in use, it should be flushed daily with isotonic NaCl solution [26]. A heparin flush solution is not recommended as no benefits are known [26], but there is a risk of heparin-induced thrombocytopenia (HIT) and incompatibilities.

In 1993, Raad et al. [27] described the non-tunnelled silastic catheter as a safe and economical alternative to the surgically implanted systems (tunnelled and port catheters). Port systems are totally implantable venous silicone or polyurethane catheters with subcutaneous reservoir chambers made of titanium or ceramic. The port membrane is made of silicone, and is only punctured with special port cannulae (non-coring port needles). It is recommended that the port needle be replaced every third to seventh day in patients receiving home PN with cyclical nutritional application. The transparent dressing should be replaced at similar intervals [28], [29], [30], [31], [32]. If no nutrient solution and only drugs (cytostatic) are administered via the port, the port needle can be left in situ for 2 weeks [33], [34], [35]. Extremely good long-term usability and high patient acceptance have been observed with correct handling [36]. Numerous prospective, non-randomised studies show a drop in the infection rate when using subcutaneous port systems [37], [38]. The tunnelled CVC (Broviac/Hickman) should be preferred over the port system for long-term PN administration in children and teenagers because relatively large flush volumes are required to flush the infusion chamber.

In a prospective cohort study, the instillation of minocycline ethylene diamine tetraacetate (M-EDTA) (port lock) significantly reduced rate of infections and thrombosis in children [39].

**Access sites/catheter position**

- In adults, the subclavian vein is preferred over the internal jugular vein or any other access site with respect to infection risk (A).
- In paediatric patients, access through the groin results in comparable infection rates that other access sites (B).
- PN solutions should be administered through a CVC with its tip positioned in the superior vena cava (C).

**Commentary**

Clinical research data are still limited with regard to the insertion site [40], [41]. Percutaneously inserted catheters should usually be placed in the superior vena cava. In adults, femoral catheters correlate with an increased risk of thrombosis and catheter-related sepsis and are, therefore, inappropriate for the administration of PN solutions [42], [43], [44], [45], [46], [47], [48], [49], [50], [51], [52]. Access to the superior vena cava can be achieved through the internal jugular vein, subclavian vein or a peripheral vein in the arm. Catheters placed through the jugular vein are associated with an increased rate of local haematomas, arterial damage and catheter-associated infections as compared to subclavian and femoral catheters [53], [54], [55], [56], [57], [58]. On the other hand, subcutaneous catheters are associated with an increased risk of pneumomotorax as compared to jugular catheters [13], [14], [54], [59], [60], [61]. It has not been conclusively determined whether the tip of the catheter is better positioned in the superior vena cava or in the right atrium [62], [63], [64], [65]. However, pericardial tamponades, cardiac arrhythmia, heart lesions and thromboses have been described when the catheter tip has been positioned in the atrium, rendering this an obsolete position.

The prospective randomised study by Cowl et al. [65] compared 102 patients receiving PN through a subclavian catheter compared to peripherally inserted CVCs. The study concluded that peripherally inserted CVCs are associated with a significantly higher rate of thrombophlebitis and placement problems. No differences have been
recorded regarding rate of infection, catheter dislocation and occlusions. These results are in line with those of other authors [66], [67], [68]. Studies in paediatric patients have shown a lower incidence of mechanical complications with access through the groin, and the rate of infection is similar to that of non-femoral access [69], [70], [71].

Control of catheter position

• An x-ray examination should be carried out after every CVC placement, if the subclavian venous access route is used, or if there were any complications with regard to implantation, or if no alternative procedure can be used to verify the catheter position (B).
• Ultrasound-controlled catheter positioning significantly reduces the rate of complications associated with cannulation (A).
• ECG-controlled CVC placement represents a safe method (A).

Commentary

Fluoroscopic control permits immediate correction of the catheter position in the superior vena cava [72], but is no longer recommended due to the relatively high radiation exposure. A radiological confirmation to ensure correct position of a CVC is recommended, by some authors, before commencing PN [73], [74], [75]. Various meta analyses have shown that ultrasound-guided CVC insertion via venous cannulation is clearly superior to conventional standard catheter placement, which uses fixed anatomical reference points, with regard to the rate of success and complications [76], [77], [78], [79], [80], [81]. Another method for confirming the position of the catheter tip in the superior vena cava or the right atrium is to use electrocardiographically guided placement [82], [83], in which a fluid-filled catheter or the retracted guide wire [83], [84] are used as an electrode for intravascular ECG-guidance [85], [86], [87]. Prerequisites are a sinus rhythm and an ECG device authorised for intracardial ECG-guidance. The procedure is not recommended limited for use in left-sided internal jugular vein cannulation because of limited accuracy [88]. Watters et al. [89] compared 1236 ECG-controlled placements with 586 fluoroscopically-controlled CVC placements. Radiological thorax monitoring resulted in an optimum catheter position in both groups [89]. Other studies (partly randomised, prospective) show that ECG-guided CVC placement is a safe method [90], [91], [92], [93].

Material-related issues

• Catheter material, catheter design, mechanical properties and anti-infectious potential correlate with the rate of complications (A).

Commentary

There are strict requirements regarding the materials used for venous catheters. Catheters must be manufactured from tissue-friendly material, must have a length classification and be X-ray opaque. Generally, every CVC represents a foreign body that can result in inflammation, formation of thrombosences, and infections. The catheter material may increase thrombogenicity which can result in catheter colonisation and catheter-associated infections [94], [95]. Special attention should be paid to potential reactions of incompatibility to the material or coatings. The associated thrombogenicity and contamination rate, due to physicochemical reactions, is high in catheters made of PVC, polypropylene or polyethylene but low in coated polyurethane catheters [62], [96], [97], [98], [99]. Catheters with a rough surface make it easier for microorganisms to attach themselves (especilly coagulase-negative staphylococci, Pseudomonas aeruginosa and Acinetobacter calcoaceticus) [62], [94], [100], [101]. Some candida species can produce mucous in the presence of glucose-based solutions which enables fungal pathogens to attach themselves easily, and explains the high rate of infection [102]. More recent data on heparin-coated CVCs show positive results regarding the reduction of CVC colonisation by microorganisms [102], [103], [104], [105]. A few isolated cases of heparin-induced thrombocytopenia (HIT) using heparin-coated pulmonary catheters and CVCs have been described in literature [106], [107]. The catheter used for central venous access should be as thin as possible and the lumen of the analogous vein should be as large as possible. The rate of infection with CVC was reported increases with the number of CVC lumina [108], [109], [110], [111], [112], but there are also studies showing no increased infection risks with multi-lumen catheters, especially if PN is administered through a separate lumen and no blood samples are taken via the CVC [52], [113], [114], [115]. As short intravascular length of the CVC catheter and limited venous wall contact appear preferable.

Hygiene measures

• Rigorous asepsis must be applied during CVC insertion (use of mask, cap, sterile gown, sterile gloves).
• Prior to the CVC insertion, the insertion site should be disinfected, preferably with chlorhexidine (B).
• Antibiotic prophylaxis and the use of antibiotic-containing creams are not recommended for CVC insertion (B).

Commentary

Evidence-based measures for the prevention of catheter-related infections in PN have been reviewed by Attar et al. [116] and O’Grady et al. [13]. Their recommendations are to wear a sterile cap, mask, gown and gloves after hand disinfection, to sufficiently disinfect the skin at the
insertion site (at least for 30 seconds with 2% chlorhexidine) as well as to use a sufficiently large, sterile drape for the cannulation site [117], [118]. The importance of team training in CVC handling is emphasised [13], [119], [120].

Skin disinfection with a 2% chlorhexidine gluconate aqueous solution reduced the colonisation rate by microorganisms compared to 10% polyvidon-iodine solution or 70% alcohol (residual effect of chlorhexidine) [118]. A randomised, prospective study showed that other chlorhexidine preparations (e.g. 0.5% tincture) are not more effective than the 10% polyvidon-iodine solution with regards to catheter colonisation [121]. In a study on newborns, a 0.5% chlorhexidine reduced the catheter colonisation rate more effectively than polyvidon-iodine solutions [122]. A multicentric study confirmed that a chlorhexidine-impregnated polyurethane foam over the catheter exit site reduces the risk of CVC colonisation and infection [123].

Antibiotic prophylaxis during catheter insertion, for prevention of line-induced infections, is not useful [61], [124], [125], [126]. The prophylactic use of antibiotic-containing creams promote resistant flora and fauna, and should, therefore, not be used [20], [127]. No difference has been observed in catheter-associated infections when it was covered with gauze or transparent film [20].

**Covering the catheter insertion site**

- Sterile gauzes or sterile, transparent, semi-permeable films should be used to cover the catheter insertion site (A).

**Commentary**

A large-scale study has compared gauze dressings and transparent film dressings in peripheral venous access. The results showed a comparable incidence of phlebitis and catheter colonisation [98]. This data indicates that transparent film dressings can remain on the insertion site throughout the duration of the intravenous therapy, without the risk of increasing thrombophlebitis [98]. A meta-analysis confirmed similar results for gauze and film dressing with regards to catheter-associated risk of infection in CVC. Film dressings could, however, result in damp patches and theoretically promote infections [128]. Well-healed insertion sites from tunneled catheters require no dressing. A gauze dressing should, preferably, be used if the catheter insertion site is bleeding or oozing [20], [129], [130], [131], [132]. dressings that have become wet/damp or loosened should be immediately replaced [61], [129], [130].

The recommendation for preferentially using alcohol-based skin disinfectants (fast-acting, positive effect) when changing the dressing has to be evaluated against the warnings of numerous catheter manufacturers regarding potential damage to catheter materials and induction of breaks by such disinfectants.

**Catheter care**

- Catheter care in patients with PN should be carried out by specially trained staff, according to define standards of care (B).

**Commentary**

A reduction in catheter-associated infections can be achieved by specifically trained personnel (training on indications, insertion and care), and by minimising manipulation of the catheter [61], [119], [133], [134], [135], [136]. Disinfection must be carried out in accordance with standards of hygiene prior to any manipulation of the catheter cuff or catheter [20], [21], [137], [138], [139], [140], [141], [142].

**CVC changes**

- CVC changes should not be performed routinely, and if an infection is suspected, no guide wire should be used for changing a CVC (A).

**Commentary**

Prophylactic catheter changes over the guide wire do not result in a drop in the risk of catheter-associated infections [143], but in an increase [110]. A CVC should not be routinely changed [13], [114], except for a CVC inserted under emergency conditions which should be reinserted after the patient’s condition has been stabilised. A CVC should be replaced when a local infection occurs at the insertion site, or if a catheter-associated bloodstream infection is suspected, but under such conditions a guide wire technique should not be used [13].

**Special catheters**

- Antibiotic or silver-coated catheters should only be used in at-risk patients and high-risk care situations (A).

**Commentary**

The rate of catheter-associated infections is reduced when using CVCs impregnated with chlorhexidine and silver sulfadiazine or with minocycline and rifampicin as compared to untreated catheters [20], [118], [144], [145]. A meta analysis outlines the infection-related benefits of a CVC impregnated with chlorhexidine-silver sulfadiazine on the exterior [103], [146], [147], [148]. Catheters coated with minocycline/rifampicin on the inside and outside performed even better in a randomised study [146], [149], [150], [151], [152], [153]. There are also positive results with silver-impregnated catheter systems [154], [155], [156].

Coated catheters should be used if the CVC is required for more than 5 days, and there is also a high risk of infection [13]. The slightly higher costs no longer presents...
a plausible argument against general use in at-risk patients [150], [157]. There is an indication for coated catheters in these at-risk patient groups: critically-ill patients, patients with compromised immune systems, newborns, infants and children [154].

Anticoagulation

- A low-dosed oral prophylactic anticoagulant should be administered to patients with home PN (B).

Commentary

Clinically relevant catheter-associated thromboses are late complications of long-term PN [63], [64], [65]. Catheter occlusions can occur because of the generation of fibrin or thrombin build-up or partial or total parietal thrombosis [158]. Two studies indicated that heparin-coated CVCs showed disadvantages regarding the potential for developing thrombosis [159], [160]. Prophylaxis with low-dosage warfarin showed a drop in the risk of thrombosis [161], [162], but not in oncology patients [163]. The favourable effect of warfarin (dose: 1 mg/day) is confirmed in the systematic review by Klerk et al. [164], but it is not confirmed for heparin [165].

Filters

- The use of in-line filters for removing particles is recommended for at-risk groups (children, immune-suppressed patients) but controversial in patients who are not at increased risk (B).

Commentary

Infusion solutions can be contaminated with particles through the manufacturing process, from the container, or during the transportation or storage process. Mixing macronutrients with electrolytes, trace elements and vitamins can result in further particle contamination (incompatibility problems). Patients receiving PN are exposed to potential contamination through container materials and administration equipment (e.g. plastic particles) as well as the unintentional introduction of bacteria and precipitates. The use of filters during PN administration is effective for the mechanical removal of larger particles, precipitates, bacteria, fungi, larger lipid particles and air [166]. However, there has not been an adequate study to date which confirms that the use of in-line filters significantly reduces the rates of catheter-associated infection [20].

The greatest concern regarding particles introduction relates to AIO admixtures containing calcium phosphate precipitates, which can cause diffuse microvascular lung embolisms [167]. Precipitates are usually not visible due to the lipid content. Calcium hydrogen phosphate is often highly-concentrated, having better solubility at 2–8°C than at 37°C, which questions the reliability of filtration. Ball et al. analysed particle contamination in “ready to use” application systems. Two admixture samples were taken from the infusion set immediately before being administered to the patient and one sample was then filtered. Both samples were evaluated microscopically. The results showed that the unfiltered sample contained significantly more particles [168].

Bethune et al. [166] recommend the use of filters in the administration of PN to the following at-risk patient groups: patients with total and/or prolonged PN, patients with weak immune systems, newborns and children. In the paper of Ball et al. [168] in-line filters are recommended for all patients receiving PN. The in-line filter should be placed as close to the patient as is practical. A 1.2 µm filter is used for lipid-containing AIO admixtures and should be changed every 24 hours. A 0.2 µm filter can only be used for non-lipid-containing infusion solutions and should only be replaced after 96 hours [169]. Filters themselves can, however, also cause problems (e.g. occlusions, adsorption of PN components like micro elements and drugs, cost of filters).

Currently, there is no proof that in-line filters have any significant influence on the rate of catheter-associated sepsicaemia [170]. Therefore, no recommendation can be made on their routine use for infection prevention. There are no legally binding rules for using in-line filters in PN. Guidance by the Robert Koch Institute [61] on using in-line filters argues against the routine use of such filters for infection prevention purposes, but it does not refer in any detail to particle infiltration.

Oclusions of the CVC or port system: measures

- CVC occlusions can be caused by blood clots, precipitations and/or residues of PN solution components, or drugs administered (A).
- Isotonic NaCl solution should be instilled as an initial measure (A).

Commentary

Catheter occlusion is the most frequent non-infectious complication. Understanding and correctly identifying the potential aetiologies leading to occlusion is extremely important for the treatment strategy [171]. Occlusions can occur in the form of blood clots or due to fibrin residues, especially after blood samples have been taken via the catheter or port systems. As an initial measure in CVC occlusions, NaCl (0.9%) should be injected after first aspirating the contents of CVC applying slight pressure. This procedure should be repeated if not initially successful. If the catheter remains blocked, it should be flushed with urokinase or RT-Pase (5000 IE/mL) (and left to work for 30–60 minutes), especially if there is a suspicion of a blood clot [172], [173], [174]. The catheter should be replaced if none of these measures are successful.

In individual cases, it is possible that tiny amounts of blood stick to the catheter wall and cannot be removed
even through intensive flushing. This is an ideal breeding ground for bacteria and can result in the colonisation of the catheter system [175], [176]. If no blood sample had been taken from the occluded system, then it must be assumed that an occlusion has probably occurred due to residue from the nutrient solution components. Lipid residues can result in CVC occlusions. These usually take a few days to form [177]. In these cases, it may be effective to instil sodium hydroxide (NaOH: 0.1 mmol/ml, 0.1 M, pH 13) [178]. Flushing with alcohol (ethanol 96%) should not be carried out, as according to silicone catheter manufacturers, alcohol immediately changes the surface of such catheters. Insoluble precipitates develop with the administration of drugs and electrolytes like calcium or phosphates. Precipitates can be caused by incompatibilities between these components e.g. by the formation of insoluble crystals [179]. Calcium phosphate precipitates are of special significance, and are influenced by various factors in the admixture like amino acid composition, relative calcium and phosphate content, pH etc. [180], [181]. A subcutaneously implanted permanent catheter, which is occluded due to insoluble precipitates, can be potentially re-utilised by pH changes in the PN solution [182], [183], [184], [185]. Bicarbonate is very incompatible, and should not be added.

Infection of the CVC or port system

Flow diagram on suspicion of catheter-induced bloodstream infection (see Figure 1) [186], [187], [188], [189].

- If catheter infection is suspected peripheral blood-culture samples, and culture samples from each catheter lumen should be taken simultaneously (A).
- Removal of the catheter should be carried out immediately when there are pronounced signs of local infection at the insertion site and/or clinical suspicion of catheter-induced sepsis (A).

Commentary

Bacterial or fungal colonisation of a CVC is a potentially life threatening complication of PN as an infection of the vascular bed with the risk of complications such as septic thrombosis, infectious colonisation of other organs and endocarditis [190]. Catheter-related sepsis occurs in 5–8% of 1000 patient days and is associated with increased morbidity, mortality and medical costs [20], [127], [191], [192].

If catheter infection is suspected and any resulting complications, the guidelines for antimicrobial therapy for catheter infections, which have been drawn up by the Paul Ehrlich society, should be observed.

It is not always easy to diagnose a catheter-associated infection by using only clinical parameters. In order to substantiate the suspected diagnosis, CVC blood cultures (in multi-lumen catheters, two blood-culture samples drawn from each catheter lumen) [193] and peripherally drawn blood cultures (collected from two separate venous cannulation sites) must be obtained (Figure 1); they should be taken at a maximum of 2 hours apart [187], [188], [189], [194]. However, the decision to remove the catheter (with the exception of subcutaneously implanted permanent catheters [195]) should be taken according to clinical criteria, and does not depend exclusively on the results of the microbiological tests.

The catheter must be removed if there are clear and definitive signs of local infection (e.g. purulent secretion at the exit site). Although, the removed catheter tip can become contaminated by this procedure, a routine microbiological test should still be carried out. Systemic antibiotic treatment (AB) should be started and adapted, if necessary, after receiving the culture and antibiotic sensitivity results. In exceptional cases, and in the absence of an immediate threat (subclinical infection), treatment with systemic antibiotics can be attempted without removing the catheter, especially if the removal of the catheter (special subcutaneously implanted permanent catheter) or the resulting consequences are likely to be problematic [20]. Potential advantages or disadvantages of catheter removal should be considered in decision-making in individual patients, e.g. those on long-term home PN [196], [197].

In the absence of local signs of infection and in clinically stable patients (subclinical infection), the catheter is left in situ temporarily. Systemic antibiotic therapy should be provided and PN continued. In patients with signs of acute sepsis (acute rise in temperature with new clinical symptoms), organ dysfunction and/or haemodynamic instability (e.g. systolic blood pressure <90 mmHg or drop in systolic blood pressure of ≥40 mmHg relative to initial value, or a mean arterial pressure <60 mmHg, or the need for blood pressure lowering drugs), the catheter must be removed. The tip should be sent for microbiological tests and a new catheter inserted at another appropriate site [198]. In these cases, a systemic antibiotic therapy must be commenced. Guidelines are available regarding further adjuvant therapy for sepsis (diagnostic and therapy of sepsis – no. 079/001 – http://www.awmf-leitlinien.de/)

Evaluation of blood culture results

If peripheral blood cultures are negative with subclinical signs of infection, but blood cultures from the CVC are positive, and if other sources of inflammation can be excluded or are unlikely from a clinical point of view, the CVC should be removed and the patient treated with antibiotics. If blood cultures drawn from both the peripheral veins and CVC are positive, or there are subclinical signs of infection, a temporary (non-tunnelled) CVC should always be removed. This particularly applies to patients with artificial heart valves [199], [200], [201] and to infections with Staphylococcus aureus or candida species. Systemic antibiotic therapy should also be commenced [202], [203], [204]. If there are only subclinical signs of infection in patients with tunnelled CVCs, as in port sys-
Figure 1: Procedure in case of suspected central venous catheter related systemic infection

- **Suspicion of catheter-induced bacteraemia or fungaemia**
  - Blood cultures peripherally and from each catheter lumen
  - Definitive signs of local infection (e.g., purulent secretion at the exit site)
  - No or questionable signs of local infections
  - Haemodynamic instability in the patient (drop in systolic blood pressure, catecholamines required) and/or signs of acute sepsis with acute rise in temperature
  - Clinically stable patient no acute rise in temperature
  - Remove CVC
  - Evaluate antibiotic therapy
  - CVC is to be left in situ
  - Evaluate antibiotic therapy

- **Blood culture sample negative & CVC-cultures negative**
  - CVC is to be left in situ.
  - Search for other causes of infections

- **Blood culture sample negative & CVC-cultures positive ≥15 CFU**
  - CVC is to be left in situ.
  - Evaluate antibiotics therapy.
  - In CVC-colonisation with Staph. aureus or candida species & patients with valvular heart disease
  - Continuous monitoring of infection.
  - Monitoring & blood culture samples at regular intervals
  - Low risk
    - Uncomplicated infection
      - With coagulase-negative staph
      - CVC can be left in situ.
      - Start with systemic antibiotic
      - Non-tunnelled CVCs
      - Remove CVC
      - Start with systemic antibiotics
  - Moderate risk
    - Uncomplicated infection
      - With staph. aureus or candida species
      - Tunnelled CVCs or port-systems
      - Evaluate antibiotic lock treatment.
      - Start with systemic antibiotics
  - High risk
    - Complicated infection
      - Hypertension, organic hypoperfusion
      - Persistent fever or bacteraemia 48 h after start of antibiotic therapy
      - Septic thrombosis, septic embolism or endocarditis
      - Patient with artificial heart valve
      - Tunnel or port-system
      - Remove CVC
      - Start with systemic antibiotics
tems, the situation should be monitored. However, a supplementary antibiotic lock treatment and systemic antibiotic therapy should be started [205], [206]. Surgical removal of the port system must be considered if these measures have no effect. Complicated infections with acute symptoms present high-risk situations regardless of blood culture results [207], [208], [209], [210]. In such cases the catheter must be removed as quickly as possible and systemic antibiotic therapy started, even before the blood culture results are received [202], [208], [209], [210], [211]. This particularly applies to secondary complications (septic thrombosis, septic embolisms or endocarditis), and also inpatients with tunnel or port system infections or with artificial heart valves [202], [207]. In addition to the systemic antibiotics and within the framework of an anticipative strategy, a further antibiotic lock treatment can be applied to tunneled CVCs or port systems and intraluminal catheter colonisation with staphylococci, enterobacteriaceae, gram-negative bacteria or fungi in the absence of blood culture infection [212], [213], [214]. A series of studies have shown that aminoglycosides or penicillin can have a favourable effect, similar to expensive third generation cephalosporins, leading to a drop in bacterial colonisation [215], [216], [217], [218]. Positive clinical experiences have been observed with the administration of vancomycin (3 ml: 2 mg/ml) or a mixture of garamycin (0.5 mg/ml) and vancomycin (1.0 mg/ml) [219], [220].

Henrickson et al. randomised 126 paediatric oncological patients with tunneled CVCs to a prophylactic lock treatment using three substances [221]. The first patient group received heparin (10 U/ml), the second group received heparin and vancomycin (25 µg/ml), and the third group received heparin, vancomycin and ciprofloxacin (2 µg/ml). The use of vancomycin-ciprofloxacin significantly reduced catheter-associated infections relative to the group receiving only heparin (p=0.005). A similar beneficial effect was observed by using vancomycin lock treatment (p=0.004). An antibiotic lock solution does not represent a routine procedure, but makes sense in patients requiring long-term access, and if there are potential problems regarding CVC reinsertion [212], [218].

**Peripheral venous access**

- In adult patients, PN through periperal venous access can be carried out if the PN is indicated for a short period (max. 7–10 days) of time and no hyperosmolar solutions (>800 mosm/L) or solutions with a high titration acidity or alkalinity (bicarbonate, TRIS-buffer) are used (B).
- A peripheral venous catheter (PVC) in adults can remain in situ for as long as it is clinically required unless there are signs of inflammation at the insertion site (A).

**Commentary**

Peripheral venous access (PVC) is associated with less complications than central venous access [222], [223]. PN administered via PVCs can only be used as additional nutritional support or as a temporary measure, as large volumes are required to deliver the required nutrients. Peripheral administration of PN should last for no more than 7–10 days as the rate of complications increases after this time period [224], [225], [226], [227]. There is no general consensus regarding the optimum PN-composition, infusion technique or pharmacological supplements, best suited to PVCs, in peripheral PN. In the absence of lipids, a limit of 800 mosm/L including potential electrolyte supplements should be adhered to. The vein quality of the patient also has to be taken into consideration. Thrombophlebitis is one of the most significant complications limiting peripheral PN. There are many factors involved in its pathogenesis. The incidence of thrombophlebitis depends on osmolarity, pH value and infusion speed of the PN solution [228], [229], [230]. Problematic substrates are glucose, amino acids and electrolytes. Earlier studies have shown that infusion solutions containing glucose and crystalline amino acids rarely resulted in phlebitis despite an osmolarity of >600 mosmol/L [231], [232]. The glucose concentration should not exceed 125 g/L [233]. A maximum osmolarity of 800–1000 mosmol/L is recommended.

No link between hyperosmolality and phlebitis has been observed in lipid-based mixtures. Kane et al. [234] randomised 36 patients for the peripheral intake of nutrient solutions with an osmolarity of between 1200 and 1700 mosmol/L. They found no difference in the incidence of phlebitis, although this either could be related to the catheter diameter and/or the flow rate. Williams et al. [235] documented similar results for lipid-based solutions with 650 mosm/kg or 860 mosm/kg. A phlebitis rate of 7–26% was recorded by McMahon et al. [225], [227], [236], [237] when lipid-based nutrient solutions with an osmolarity over 1100 mosmol/L were administered. The pH value of commercial nutrient solutions is approximately 5 to 6. The acidity is caused by the amino acids and glucose degradation products which are produced during sterilisation [238]. The frequently used PN bags made of ethylene-vinyl-acetate (EVA) are permeable to air; this allows for the oxidation of nutrients, for example, of glucose to gluconic acid [239]. Experimental studies showed a significant correlation between increased acidity and an incidence of phlebitis in different infusion solutions [229], [240], [241]. Adding a neutralising buffer to infusion solutions with crystalloids (normal pH 4.0–6.5) resulted in a reduction in the rate of phlebitis [238]. There are, however, no significant clinical studies supporting the routine use of buffer supplements in peripheral PN. Furthermore, the effects of these supplements on the stability of PN would be difficult to assess. In addition, the amino acid mixtures themselves have a buffer effect (pK values).
While an increased rate of phlebitis and infection at a LOS of over 3 days was postulated earlier [99], [242], more recent studies show that the time-specific risk of an obstruction, phlebitis and catheter colonisation remains the same even in longer LOS [243], [244], [245]. Peripheral venous catheters can, therefore, remain in place as long as they are clinically required [61], [243]. In children, peripheral access may be left for the total duration of intravenous administration and only be changed if complications arise [245], [246], [247], [248]. The risk of phlebitis is lower when the cannula is placed on the back of the hand compared to venous access sites in the wrist or upper arm [249].

Notes

This article is part of the publication of the Guidelines on Parenteral Nutrition from the German Society for Nutritional Medicine (overview and corresponding address under http://www.egms.de/en/gms/2009-7/000086.shtml). English version edited by Sabine Verwied-Jorky, Rashmi Mittal and Berthold Koletzko, Univ. of Munich Medical Centre, Munich, Germany.

References

1. Krzywda EA, Andris DA, Edmiston CE. Catheter infections: Diagnosis, etiology and treatment and prevention. Nutr Clin Pract. 1999;14:178. DOI: 10.1177/08845369901400405

2. Chung DH, Ziegler MM. Central venous catheter access. Nutrition. 1998;14:119-23. DOI: 10.1016/S0899-9007(97)00228-1

3. Meadows N. Monitoring and complications of parenteral nutrition. Nutrition. 1998;14:806-8. DOI: 10.1016/S0899-9007(98)00089-6

4. Lederle FA, Parenti CM, Berskow LC, Ellingson KJ. The idle intravenous catheter. Ann Intern Med. 1992;116(9):737-8.

5. Parenti CM, Lederle FA, Impola CL, Peterson LR. Reduction of unnecessary intravenous catheter use; Internal medicine house staff participate in a successful quality improvement project. Arch Intern Med. 1994;154(16):1829-32.

6. Gebauer B, Teichgräber UK, Podrabsky P, Beck A, Wagner HJ. Ultraschall- und durchleuchtungs-gesteuerte Implantation peripher inserierter zentral-venöser Katheter (PICC) [Ultrasound and Fluoroscopy-guided Implantation of Peripherally Inserted Central Venous Catheters (PICCs)]. Fortschr Röntgenstr. 2004;176:386-91. DOI: 10.1055/s-2004-812737

7. Duerksen DR, Papineau N, Siemens J, Yaffe C. Peripherally inserted central catheters for parenteral nutrition: a comparison with centrally inserted catheters. JPN J Parenter Enteral Nutr. 1999;23:85-9. DOI: 10.1177/014860719920300285

8. Kumar M, Amin M. The peripherally inserted central venous catheter; friend or foe? Int J Oral Maxillofac Surg. 2004;33:201-4. DOI: 10.1054/joms.2003.0464

9. Nessler R. Spezielle Punktionstechnik für “zentrale” Venen [Technik nach Seldinger oder indirekte Technik] [Special technique for the catheterization of “central” veins (Seldinger’s or indirect technique)]. Prakt Anaesth. 1978;13:99-102.

10. Peters JL, Armstrong R. Air embolism occurring as a complication of central venous catheterization. Ann Surg. 1978;187:375-6. DOI: 10.1097/00000658-197804000-00005

11. Stow PJ, Burrows FA, Berthelsen PG, Stöber H, Durrant STS, Rahemtulla A, et al. Central venous catheterisation. Lancet. 1986;328:974-5. DOI: 10.1016/S0140-6736(86)90623-9

12. Belani KG, Buckley JJ, Gordon JR, Castaneda W. Percutaneous cervical central venous line placement: a comparison of the internal and external jugular vein routes. Anesth Analg. 1980;59(1):40-4.

13. O’Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, Masur H, McCormick RD, Mermel LA, Pearson ML, Raad II, Randolph A, Weinstein RA. Control and Prevention Guidelines for the prevention of intravascular catheter-related infections; Centers for Disease. MMWR Recomm Rep. 2002;51(RR-10):1-29.

14. Polderman KH, Gibbes AR. Central venous catheter use; Part 2: infectious complications. Intensive Care Med. 2002;28(1):18-28.

15. Raad I, Umphrey J, Khan A, Truett LJ, Bodey GP. The duration of placement as a predictor of peripheral and pulmonary arterial catheter infections. J Hosp Infect. 1993;23:23-26. DOI: 10.1016/0195-6701(93)90126-K

16. Richet H, Hubert B, Ntemberg G, Andremont A, Bao-Hoi A, Ourbak P, Galicier C, Veron M, Boissivan A, Bouvier AM, et al. Prospective multicenter study of vascular-catheter-related complications and risk factors for positive central-catheter goodwells in intensive care unit patients. J Clin Microbiol. 1990;28(11):2520-5.

17. Fuchs PC, Gustafson ME, King JT, Goodall PT. Assessment of catheter-associated infection risk with the Hickman right atrial catheter. Infect Control. 1984;5(5):226-30.

18. Thomas JH, MacArthur RI, Pierce GE, Hermreck AS. Hickman-Browiac catheters: Indications and results. Am J Surg. 1980;140:791-6. DOI: 10.1016/0002-9610(80)90119-1

19. Snyderman DR, Murray SA, Kornfeld SJ, Majka JA, Ellis CA. Total parenteral nutrition-related infections: Prospective epidemiologic study using semiquantitative methods. Am J Med. 1982;73:695-9. DOI: 10.1016/0002-9343(82)90412-0

20. Mermel LA. Prevention of intravascular catheter-related infections. Ann Intern Med. 2000;132(5):391-402.

21. Bjarnason K, Field J, Weston V, Stanga Z. Venesecusion for blood culture: trained nurses achieve same or lower contamination rates than doctors. Clin Nutr. 2002;21:10.

22. O’Grady NP, Alexander M, Dellinger EP, Gerberding JL, Heard SO, Maki DG, et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control. 2002;30:476-89. DOI: 10.1067/mic.2002.129427

23. Hanna HA, Raad I. Blood products: a significant risk factor for long-term catheter-related bloodstream infections in cancer patients. Infect Control Hosp Epidemiol. 2002;22:165-6. DOI: 10.1086/501885

24. Barrett BB, Andersen JW, Anderson KC. Strategies for the avoidance of bacterial contamination of blood components. Transfusion. 1993;33:228-33. DOI: 10.1046/j.1537-2995.1993.33393174449.x

25. Timsit JF, Sebille V, Farkas JC, Misset B, Martin JB, Chevret S, et al. Effect of subcutaneous tunneling on internal jugular catheter-related sepsis in critically ill patients: a prospective randomized multicenter study. JAMA. 1996;276:1416-20.

26. Shaffer JL, Bakker H, Bozzetti F, Ladedoged K, Leon-Sanz M, Messing B, et al. A European survey on management of catheter-related complications in home parenteral nutrition. Clin Nutr. 1997;16:42. DOI: 10.1016/S0261-5614(97)80196-3
27. Raad I, Davis S, Becker M, Hohn D, Houston D, Umphrey J, et al. Low infection rate and long durability of nontunneled silastic catheters. A safe and cost-effective alternative for long-term venous access. Arch Intern Med. 1993;153:1791-6.

28. Chang L, Tse J, Huang SJ, Shih CC. Evaluation of infectious complications of the implantable venous access system in a general oncologic population. Am J Infect Control. 2003;31:34-9. DOI: 10.2016/mic.2003.29

29. Raad I, Hanna AW, Awad A, Aralahan AW, Bivins C, Khan A, et al. Optimal frequency of changing intravenous administration sets: is it safe to prolong use beyond 72 hours? Infect Control Hosp Epidemiol. 2001;22:136-9. DOI: 10.1086/501879

30. Maki DG, Botticelli JT, Lefroy ML, Thielle TS. Prospective study of replacing administration sets for intravenous therapy at 48- vs 72-hour intervals. 72 hours is safe and cost-effective. JAMA. 1987;258:1777-81.

31. Matlow AG, Kita I, Kirpalani H, Chapman NH, Corey M, Perlman M, et al. A randomized trial of 72-versus 24-hour intravenous tubing set changes in newborns receiving lipid therapy. Infect Control Hosp Epidemiol. 1999;20:487-93. DOI: 10.1086/501657

32. Sitges-Serra A, Linares J, Perez JL, Jaurrieta E, Lorente L. A randomized trial on the effect of tubing changes on hub contamination and catheter sepsis during parenteral nutrition. JPNJ Parenter Enteral Nutr. 1985;9:322-5. DOI: 10.1177/0148607185009003322

33. Nanninga AG, de Vries EG, Willems PH, Oosterhuis BE, Sleijfer DT, Hoeskstra HJ, et al. Continuous infusion of chemotherapy on an outpatient basis via a totally implanted venous access port. Eur J Cancer. 1991;27(2):147-9.

34. Milani A, Vernizzi S, Passoni C, Sociale O, Macciola F, Grimaldi C, et al. Tempo di giacenza in situ dell’ago di huber in pazienti sottoposti a chemioterapia in infusione continua: risultati di uno studio di fase II [Hub needle in situ in patients under continuous infusion chemotherapy: results of a study, Phase III]. Prof Inferm. 2000;53:71-4.

35. Karamanoglu A, Yumuk PF, Gumus M, Ekenel M, Aliustaoglu M, Selimen D, et al. Port needles: do they need to be removed as frequently in infusion chemotherapy? J Infus Nurs. 2003;26:239-42. DOI: 10.1097/00129804-200307000-00009

36. Mühlbacher S, Fasolini F. 10 Jahre Ernährungssteam am Kantonsspital Aarau (KSA): Aufgaben, Entwicklungen, Erfahrungen [The nutrition support team at the Kantonsspital Aarau (KSA): Functions, development, and experiences over a ten year period]. Viszeralchirurgie. 2000;35:69-71. DOI: 10.1055/s-2000-11232

37. La Quaglia MP, Lucas A, Thaler HT, Friedlander-Klar H, Exelby PR, Groeger JS. A prospective analysis of vascular access device-related infections in children. J Pediatr Surg. 1992;27:840-2. DOI: 10.1016/0022-3468(92)90379-L

38. Miller K, Buchanan GR, Zappa S, Cochran C, Laufenberg J, Medeiros D, et al. Implantable venous access devices in children with hemophilia: a report of low infection rates. J Pediatr. 1998;132:934-8. DOI: 10.1001/jpeds.132.6.9386-5

39. Chatzinikolaou I, Zipf TF, Hanka U, Umphrey J, Roberts WM, Sherritz R, et al. Minocycline-ethylene diamine tetraacetate lock solution for the prevention of implantable port infections in children with cancer. Clin Infect Dis. 2003;36:116-9. DOI: 10.1086/344952

40. Ivanov R, Allen J, Calvin JE. The incidence of major morbidity in critically ill patients managed with pulmonary artery catheters: a meta-analysis. Crit Care Med. 2000;28:615-9. DOI: 10.1097/00003324-200003000-00002

41. Ruesch S, Walder B, Tramer MR. Complications of central venous catheters: internal jugular versus subclavian access – a systematic review. Crit Care Med. 2002;30:454-60. DOI: 10.1097/00003324-200202000-00031

42. Bansmer G, Keith D, Tesluk H. Complications following use of indwelling catheters of inferior vena cava. J Am Med Assoc. 1958;167:1606-11.

43. Crane V. Cen venous interruption of septic thrombophlebitis. N Engl J Med. 1960;262:947-51.

44. Indar R. The dangers of indwelling polyethylene cannulae in deep veins. Lancet. 1959;1:284-7. DOI: 10.1016/S0140-6736(59)90207-7

45. Goetz AM, Wagener GM, Miller JM, Muder RR. Risk of infection due to central venous catheters: effect of site of placement and catheter type. Infect Control Hosp Epidemiol. 1998;19(11):842-5.

46. Joynt GM, Kew J, Gomersall CD, Leung VY, Liu EK. Deep venous thrombosis caused by femoral venous catheters in critically ill adult patients. Chest. 2000;117:178-83. DOI: 10.1378/chest.117.1.178

47. Mian NZ, Bayly R, Schreck DM, Bessereman EB, Richmand D. Incidence of deep vein thrombosis associated with femoral venous catheterization. Acad Emerg Med. 1997;4:1118-21. DOI: 10.1111/j.1553-7212.1997.tb03693.x

48. Durbec O, Vivandi X, Potie F, Viallet R, Albanese J, Martin C. A prospective evaluation of the use of femoral venous catheters in critically ill adults. Crit Care Med. 1997;25:1986-9. DOI: 10.1097/00003324-199712000-00014

49. Merrer J, De Jonghe B, Golliot F, Lefrant JY, Raffy B, Barre E, et al. Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. JAMA. 2001;286:700-7. DOI: 10.1001/jama.286.6.700

50. Trottier SJ, Veremakis C, O’Brien J, Auer AL. Femoral deep vein thrombosis associated with central venous catheterization: results from a prospective, randomized trial. Crit Care Med. 1995;23:52-9. DOI: 10.1097/00003324-199501000-00011

51. Harden JL, Kemp L, Mirtallo J. Femoral catheters increase risk of infection in total parenteral nutrition patients. Nutr Clin Pract. 1995;10:90-6. DOI: 10.1177/011542659501000260

52. Kemp L, Burge J, Choban P, Harden J, Mirtallo J, Flanbaum L. The effect of catheter type and site on infection rates in total parenteral nutrition patients. JPNJ Parenter Enteral Nutr. 1994;18:71-4. DOI: 10.1177/014860719401800171

53. Sznajder J, Zveibil F, Ritterman H, Weiner P, Burststein S. Central vein catheterization. Failure and complication rates by three percutaneous approaches. Arch Intern Med. 1986;146:259-61.

54. Mermei L. Central venous catheter-related infections and their prevention: is there enough evidence to recommend tunneling for short-term use? Crit Care Med. 1998;26:1315-6. DOI: 10.1097/00003324-199808000-00011

55. Mermei LA, McCormick RD, Springman SR, Maki DG. The pathogenesis and epidemiology of catheter-related infection with pulmonary artery Swan-Ganz catheters: a prospective study utilizing molecular subtyping. Am J Med. 1991;91:197S-205S. DOI: 10.1016/0002-9343(91)90369-9

56. Heard SO, Wagle M, Vijayakumar E, McLean S, Brueggemann A, Napolitano LM, et al. Influence of triple-lumen central venous catheters coated with chlorhexidine and silver sulfadiazine on the incidence of catheter-related bacteremia. Arch Intern Med. 1998;158:81-7. DOI: 10.1001/archinte.158.1.81

57. Richet H, Hubert B, Nitemberg G, Andremont A, Buu-Hoi A, Ourbak P, Gallicier C, Veron M, Boisivon A, Bouvier AM, et al. Prospective multicenter study of vascular-catheter-related complications and risk factors for positive central-catheter cultures in intensive care unit patients. J Clin Microbiol. 1990;28(11):2520-5.
73. Miller JA, Singireddy S, Malajian P, Baker SR. A reevaluation of the radiographically detectable complications of percutaneous venous access lines inserted by four subcutaneous approaches. Am Surg. 1999;65(2):125-30.

74. Fisher KL, Leung AN. Radiographic appearance of central venous catheters. AJR Am J Roentgenol. 1996;166(2):329-37.

75. Caridi JG, West JH, Stavropoulos SW, Hawkins IF Jr. Internal jugular and upper extremity central venous access in interventional radiology: is a postprocedure chest radiograph necessary? AJR Am J Roentgenol. 2000;174:363-6.

76. Randolph AG, Cook DJ, Gonzales CA, Pribble CG. Ultrasound guidance for placement of central venous catheters: a meta-analysis of the literature. Crit Care Med. 1996;24:2053-8. DOI: 10.1097/00003246-199612000-00020

77. Brass P, Volk O, Leben J, Schregel W. Zentralvenöse Punktion – nur noch mit Ultraschall? [Central Venous Cannulation – Always with Ultrasound Support?]. Anaesthesiol Intensivmed Notfallmed Schmerzther. 2001;36:619-27. DOI: 10.1055/s-2001-17671

78. Keenan SP. Use of ultrasound to place central lines. J Crit Care. 2002;17:126-37. DOI: 10.1016/j.jcrc.2002.34364

79. Wagner HJ, Teichgräber U, Gebauer B, Kalinowski M. Die transjuguläre Implantation venoser Portkathetersysteme [Transjugular implantation of venous port catheter systems]. Röfo. 2003;175:1539-44.

80. Hind D, Calvert N, McWilliams R, Davidson A, Paisley S, Beverley C, et al. Ultrasonic locating devices for central venous cannulation; meta-analysis. BMJ 2003; 327: 361 DOI: 10.1136/bmj.327.7411.361

81. Ogunkurt L, Tercan F, Kara G, Torun D, Kizilkilic O, Yıldirim T. US-guided placement of temporary internal jugular vein catheters: immediate technical success and complications in normal and high-risk patients. Eur J Radiol. 2005;55:125-9. DOI: 10.1016/j.ejrad.2004.10.004

82. Schäfer M, Reinhart K. Die Plazierung von zentralen Venenkathetern mit Hilfe der intraatrialen EKG-Ableitung [Placement of central venous catheters using intra-arterial ECG recording]. Zentralbl Chir. 1993;118:432-5.

83. McGee WT, Mallory DL, Johans TG, et al. Safe placement of central venous catheters is facilitated using right atrial electrocardiography. Crit Care Med. 1988;16:434. DOI: 10.1097/00003246-198804000-00151

84. Fritz KW, Gras C, Logemann F, Kirchhoff K. Die Positionierung des zentralen-venösen Katheters mit Hilfe des intraatrialen EKG [Positioning the central venous catheter using intra-atrial ECG]. Anaesthesiol Reanim. 1991;16(6):399-402.

85. Nakatani K, Nishikawa K, Funao T, Ikeda Y, Nakasuji K, Iida Y, et al. Accurate placement of central venous catheter - ECG-guided method vs patient height method. Masui. 2002;51(1):34-8.

86. Madias JE. Intracardiac (superior vena cava/right atrial) ECGs using saline solution as the conductive medium for the proper positioning of the saline solution catheter: is it not time to forgo the postinsertion chest radiograph? Chest. 2003;124:2363-7. DOI: 10.1378/chest.124.6.2363

87. Madias JE. Intracardiac electrocardiography via a "saline-filled central venous catheter electrocardiographic lead": a historical perspective. J Electrocardiol. 2004;37:3-8. DOI: 10.1016/j.jelectrocard.2004.03.003

88. Schummer W, Herrmann S, Schummer C, Funke F, Steenbeck J, Fuchs J, et al. Intra-atrial ECG is not a reliable method for positioning left internal jugular vein catheters. Br J Anaesth. 2003;91:481-6. DOI: 10.1093/bja/aeg308

89. Watters VA, Grant JP. Use of electrocardiogram to position right atrial catheters during surgery. Ann Surg. 1997;225:165-71. DOI: 10.1097/00000658-199702000-00004
105. Foley PL, Barthel CH, Brausa HR. Effect of covalently bound heparin coating on patency and biocompatibility of long-term indwelling catheters in the rat jugular vein. Comp Med. 2002;52(3):243-8.

106. Nasuno A, Matsubara T, Hori T, Higuchi K, Tsuchida K, Mezaki T, et al. Acute pulmonary thromboembolism induced by prophylactic heparin use and a heparin-coated catheter: a case of heparin-induced thrombocytopenia and thrombosis syndrome. Circ J. 2003;67:96-8. DOI: 10.1253/circ.67.96

107. Laster JL, Nichols WK, Silver D. Thrombocytopenia associated with heparin-coated catheters in patients with heparin-associated antiplatelet antibodies. Arch Intern Med. 1989;149:2285-7.

108. Tokars JJ, Cookson ST, McArthur MA, Boyer CL, McGeer AJ, Jarvis WR. Prospective evaluation of risk factors for bloodstream infection in patients receiving home infusion therapy. Ann Intern Med. 1999;131(5):340-7.

109. Gil RT, Kruse JA, Thill-Baharoonian MC, Carlson RW. Triple- vs single-lumen central venous catheters: A prospective study in a critically ill population. Arch Intern Med. 1989;149:1139-43.

110. Hilton E, Haslett TM, Borenstein MT, Tucci V, Isenberg HD, Singer C. Central catheter infections: single- versus triple-lumen catheters. Influence of guide wires on infection rates when used for replacement of catheters. Am J Med. 1988;94:867-72. DOI: 10.1016/0002-9343(88)90102-7

111. McCarthy MC, Shives JK, Robison RJ, Broadie TA. Prospective evaluation of single and triple lumen catheters in total parenteral nutrition. JPEN J Parenter Enter Nutr. 1987;11:259-62. DOI: 10.1017/S014860770701003259

112. Pemberton LB, Lyman B, Lander V, Covinsky J. Sepsis from triple- vs single-lumen catheters during total parenteral nutrition in surgical or critically ill patients. Arch Surg. 1986;121:591-4.

113. Ma TY, Yoshinaka R, Banaag A, Johnson B, Davis S, Berman SM. Total parenteral nutrition via multilumen catheters does not increase the risk of catheter-related sepsis: a randomized, prospective study. Clin Infect Dis. 1998;27:500-3. DOI: 10.1086/514687

114. Savage AP, Picard M, Hopkins CC, Malt RA. Complications and survival of multilumen central venous catheters used for total parenteral nutrition. Br J Surg. 1993;80:1287-90. DOI: 10.1002/bjs.1800801021

115. Mangiano R, Martin M. Safety of triple lumen catheters in the critically ill. Am Surg. 1991;57(6):597-9.

116. Attar A, Messing B. Evidence-based prevention of catheter infection during parenteral nutrition. Curr Opin Clin Nutr Metab Care. 2001;4:211-8. DOI: 10.1097/00075197-200105000-00008

117. Raad II, Hohn DC, Gilbreath BJ, Suleiman N, Hill LA, Bruso PA, Marts K, Mansfield PF, Bodey GP. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. Infect Control Hosp Epidemiol. 1994;15(4Pt1):239-43. DOI: 10.1086/514687

118. Raad II, Hohn DC, Gilbreath BJ, Suleiman N, Hill LA, Bruso PA, Marts K, Mansfield PF, Bodey GP. Prevention of central venous catheter-related infections by using maximal sterile barrier precautions during insertion. Infect Control Hosp Epidemiol. 1994;15(4 Pt 1):231-8.

119. Maki DG, Ringer M, Alvarado CJ. Prospective randomised trial of pivovodine-iodeine, alcohol, and chlorhexidine for prevention of infection associated with central venous and arterial catheters. Lancet. 1991;338:339-43. DOI: 10.1016/0140-6736(91)90479-9

120. Alonso-Echanove J, Edwards JR, Richards MJ, Brennan P, Venezia RA, Keen J, et al. Evidence of nurse staffing and antimicrobial-impregnated central venous catheters on the risk for bloodstream infections in intensive care units. Infect Control Hosp Epidemiol. 2003;24:916-25. DOI: 10.1086/502160

121. Abi-Said D, Raad I, Umphrey J, Gonzalez V, Richardson D, Marts K, et al. Infusion therapy team and dressing changes of central venous catheters. Infect Control Hosp Epidemiol. 1999;20:101-5. DOI: 10.1086/501597
121. Humar A, Ostromecki A, Direnfeld J, Marshall JC, Lazar N, Houston PC, et al. Prospective randomized trial of 10% povidone-iodine versus 0.5% tincture of chlorhexidine as cutaneous antisepsis for prevention of central venous catheter infection. Clin Infect Dis. 2000;31:1001-7. DOI: 10.1086/318145

122. Garland JS, Buck RK, Maloney P, Durkin DM, Toth-Lloyd S, Duffy M, et al. Comparison of 10% povidone-iodine and 0.5% chlorhexidine gluconate for the prevention of peripheral intravenous catheter colonization in neonates: a prospective trial. Pediatr Infect Dis J. 1995;14:510-6. DOI: 10.1097/00006454-199506000-00008

123. Safdar N, Kluger DM, Maki DG. A review of risk factors for catheter-related bloodstream infection caused by percutaneously inserted, noncuffed central venous catheters: implications for preventive strategies. Medicine (Baltimore). 2002;81:466-79. DOI: 10.1097/00005850-200211000-00007

124. Ranson MR, Oppenheim BA, Jackson A, Kambhan AG, Scarffe JH. Double-blind placebo controlled study of vancomycin prophylaxis for central catheter insertion in cancer patients. J Hosp Infect. 1990;15:95-102. DOI: 10.1016/0195-6701(90)90025-J

125. Ljungman P, Hagglund H, Bjorkstrand B, Lonqvist B, Ringden O. Perioperative teicoplanin for prevention of gram-positive infections in neutropenic patients with indwelling central venous catheters: a randomized, controlled study. Support Care Cancer. 1997;5:485-8. DOI: 10.1007/s005200050117

126. Do AN, Ray BJ, Banerjee SN, Illian AF, Barnett BJ, Pham MH, et al. Bloodstream infection associated with needleless device use and the importance of infection-control practices in the home health care setting. J Infect Dis. 1999;179:442-8. DOI: 10.1086/314592

127. Gosbell IB. Central venous catheter related sepsis: epidemiology, pathogenesis, diagnosis, treatment and prevention. Intensive Care World. 1994;11:54-9.

128. Hoffmann KK, Weber DJ, Samsha GP, Rutala WA. Transparent polyurethane film as an intravenous catheter dressing. A meta-analysis of the infection risks. JAMA. 1992;267:2072-6.

129. Maki DG, Stolz SM, Wheeler S, Merrel LA. A prospective, randomized trial of gauze and two polyurethane dressings for site care of pulmonary artery catheters: implications for catheter management. Crit Care Med. 1994;22(11):1729-37.

130. Benezra D, Kiehn TE, Gold JW, Brown AE, Turnbull AD, Armstrong DR. A randomized trial comparing Arglaes (a transparent dressing containing silver ions) to Tegaderm (a transparent polyurethane dressing) for dressing peripheral arterial catheters and central vascular catheters. Intensive Crit Care Nurs. 1998;14:187-91. DOI: 10.1016/S0964-3397(98)80512-0

131. Armstrong CW, Mayhall CG, Miller KB, Newsome HH Jr, Sugerman HJ, Dalton HP, et al. Prospective study of catheter replacement and other risk factors for infection of hyperalimentation catheters. J Infect Dis. 1988;158:808-16.

132. Nehme AE. Nutritional support of the hospitalized patient; The team concept. JAMA. 1980;243(19):1906-8.

133. Soifer NE, Borzak S, Edlin BR, Weinstein RA. Prevention of peripheral venous catheter complications with an intravenous therapy team: a randomized controlled trial. Arch Intern Med. 1998;158:473-7. DOI: 10.1001/archinte.158.5.473

134. Tomford JW, Hershey CO. The iv therapy team: impact on patient care and costs of hospitalization. NITA. 1985;8(5):387-9.

135. Sherertz RJ, Ely EW, Westbrook DM, G fledhill KS, Streed SA, Kiger B, et al. Education of physicians-in-training can decrease the risk for vascular catheter infection. Ann Intern Med. 2000;132(8):641-8.

136. Ryan JA Jr, Abel RM, Abbott WM, Hopkins CC, Chesney TM, Colley R, Phillips K, Fischer J. Catheter complications in total parenteral nutrition: A prospective study of 200 consecutive patients. N Engl J Med. 1974;290(14):757-61.

137. Sanders RA, Sheldon GF. Septic complications of total parenteral nutrition: A five year experience. Am J Surg. 1976;132:214-20. DOI: 10.1016/0002-9610(76)90050-7

138. Murphy LM, Lipman TO. Central venous catheter care in parenteral nutrition: a review. J PEN J Parenter Enteral Nutr. 1987;11:190-201. DOI: 10.1177/0148607187011002190

139. Eggimann P, Barhart S, Constantin MN, Touveneau S, Chevrolet JC, Pittet D. Impact of a prevention strategy targeted at vascular-access care on incidence of infections acquired in intensive care. Lancet. 2000;355:1864-8. DOI: 10.1016/S0140-6736(00)02291-1

140. Safdar N, Maki DG. The pathogenesis of catheter-related bloodstream infection with noncuffed short-term central venous catheters. Intensive Care Med. 2004;30:62-7. DOI: 10.1007/s00134-003-2045-z

141. Cook D, Randolph A, Kermerman P, Cupido C, King D, Soukup C, et al. Central venous catheter replacement strategies: a systematic review of the literature. Crit Care Med. 1997;25:1417-24. DOI: 10.1097/00003246-199708000-00033

142. Maki DG, Stolz SM, Wheeler S, Merrel LA. Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter; A randomized, controlled trial. Ann Intern Med. 1997;127(4):257-66.

143. Fraenkel D, Rickard C, Thomas P, Faogalal J, George N, Ware R. A prospective, randomized trial of rifampicin-minocycline-coated and silver-platinum-carbon-impregnated central venous catheters. Crit Care Med. 2006;34:668-75. DOI: 10.1097/01.CCM.0000201404.05523.34

144. Veenstra DL, Saint S, Saha S, Lumley T, Sullivan SD. Efficacy of antiseptic-impregnated central venous catheters in preventing catheter-related bloodstream infection: a meta-analysis. JAMA. 1999;281:261-7. DOI: 10.1001/jama.281.3.261

145. Jaeger K, Zenz S, Juttner B, Ruschulte H, Kuse E, Heine J, et al. Reduction of catheter-related infections in neutropenic patients: a prospective controlled randomized trial using a chlorhexidine and silver sulfadiazine-impregnated central venous catheter. Ann Hematol. 2005;84:258-62. DOI: 10.1007/s00277-004-0972-6

146. Khare MD, Bukhari SS, Swann A, Spiers P, McLaren I, Myers J. Reduction of catheter-related colonisation by the use of a silver zeolite-impregnated central vascular catheter in adult critical care. J Infect. 2007;54(2):146-50. DOI: 10.1016/j.jinf.2006.03.002

147. Benezra D, Kiehn TE, Gold JW, Brown AE, Turnbull AD, Armstrong D. Prospective study of infections in indwelling central venous catheters using quantitative blood cultures. Am J Med. 1988;85(4):495-8.

148. Darouiche RO, Raad II, Heard SO, Thornby JI, Wenker OC, Gabrielli A, et al. A comparison of two antimicrobial-impregnated central venous catheters; Catheter Study Group. N Engl J Med. 1999;340:1-8. DOI: 10.1056/NEJM199901073400101

GMS German Medical Science 2009, Vol. 7, ISSN 1612-3174
164. Klerk CP, Smorenburg SM, Buller HR. Thrombosis prophylaxis in patient populations with a central venous catheter: a systematic review. Arch Intern Med. 2003;163:1913-21. DOI: 10.1001/archinte.163.16.1913

165. Verso M, Agnelli G, Bertoglio S, Di Somma FC, Paoletti F, Ageno W, et al. Enoxaparin for the prevention of venous thromboembolism associated with central vein catheter: a double-blind, placebo-controlled, randomized study in cancer patients. J Clin Oncol. 2005;23:4057-62. DOI: 10.1200/JCO.2005.06.084

166. Bethune K, Allwood M, Grainger C, Wormleighton C. Use of filters during the preparation and administration of parenteral nutrition: position paper and guidelines prepared by a British pharmaceutical nutrition group working party. Nutrition. 2001;17:403-8. DOI: 10.1016/S0899-9007(01)00536-6

167. Lumpkin MM. Safety alert: hazards of precipitation associated with parenteral nutrition. Am J Hosp Pharm. 1994;51(11):1427-8.

168. Ball PA, Bethune KM, Fox JC, et al. Particulate contamination in parenteral nutrition solutions, still cause for concern. Clin Nutr. 1999;18:14.

169. Ball PA. Intravenous in-line filters: filtering the evidence. Curr Opin Clin Nutr Metab Care. 2003;6:318-25. DOI: 10.1097/00075197-200305000-00009

170. Newall F, Ranson K, Robertson J. Use of in-line filters in pediatric intravenous therapy. J Intraven Nurs. 1998;21(3):166-70.

171. Bethune KM, Lader M, Catterall H. Efficacy of continuous quality improvement project. Arch Intern Med. 1999;159:1632-40. DOI: 10.1001/archinte.115.6.1632

172. Boswald M, Lugauer S, Regenfus A, Braun GG, Martus P, Geis BF. Material thrombogenicity in central venous catheterization; A comparison between uncoated and heparin-coated, long antebrachial, polyethylene catheters. Acta Anaesthesiol Scand. 1998;42:112-20. DOI: 10.1111/j.1399-6576.1998.tb01736.x

173. Gale GB, O'Connor DM, Chu JY, Stanley D. Restoring patency of thrombosed catheters with cryopreserved urokinase. J Parenter Enteral Nutr. 1987;11:507-10. DOI: 10.1177/0148607187011005507

174. Rumsey KA, Richardson DK. Management of infection and occlusion associated with vascular access devices. Semin Oncol Nurs. 1995;11:174-83. DOI: 10.1016/S0749-2081(95)80027-1

175. Mühlebach S. Was der praktizierende Arzt vom Umgang mit Infusionen wissen muss [What the practicing physician must know about giving infusions?], Praxis (Bern). 2001;90(13):546-8.

176. Allwood MC, Kearney MC. Compatibility and stability of additives in parenteral nutrition admixtures. Nutrition. 1998;14:697-706. DOI: 10.1016/S0899-9007(98)80063-X

177. Stennett DJ, Gerwick WH, Egging PK, Christensen JM. Precipitate analysis from an indwelling total parenteral nutrition catheter. J Parenter Enteral Nutr. 1986;10:38-42. DOI: 10.1177/014860718801200188

178. Shulman RJ, Reed T, Pitre D, Laine L. Use of hydrochloric acid to clear obstructed central venous catheters. J Parenter Enteral Nutr. 1988;12:500-10. DOI: 10.1177/0148607188012005509
183. Duffy LF, Kerzner B, Gebus V, Dice J. Treatment of central venous catheter occlusions with hydrochloric acid. J Pediatr. 1989;114:1002-4. DOI: 10.1016/S0022-3476(89)80449-9

184. Goodwin ML. Using sodium bicarbonate to clear a medication precipitate from a central venous catheter. J Vasc Access N. 1999;1:23.

185. Holcombe BJ, Forlon-Lynn S, Garmhausen LW. Restoring patency of long-term central venous access devices. J Intraven Nurs. 1992;15(1):36-41.

186. Siegmam-Igra Y, Anglím AM, Shapiro DE, Adal KA, Strain BA, Ferr AM. Diagnosis of vascular catheter-related bloodstream infection: a meta-analysis. J Clin Microbiol. 1997;35(4):928-36.

187. Meruelo LA, Ferr AM, Sherertz RJ, Raad II, O'Grady N, Harris JS, et al. Guidelines for the management of intravenous catheter-related infections. Clin Infect Dis. 2001;32:1249-72. DOI: 10.1086/320001

188. Raad II, Hanna HA. Intravascular catheter-related infections: new horizons and recent advances. Arch Intern Med. 2002;162:871-8. DOI: 10.1001/archinte.162.8.871

189. Rijnders BJ, Peetermans WE, Verwaest C, Wilmer A, Van Wijngaarden E. Watchful waiting versus immediate catheter removal in ICU patients with suspected catheter-related infection: a randomized trial. Intensive Care Med. 2004;30:1073-80. DOI: 10.1007/s00134-004-2211-x

190. Krzywda EA, Edmiston CE Jr. Central venous catheter infections: Clinical aspects of microbial etiology and pathogenesis. J Infus Nurs. 2002;25:29-35. DOI: 10.1097/00129804-20021000-00006

191. Forchielli ML, Gura K, Anessi-Pessina E, Richardson D, Cai W, Lo CW. Success rates and cost-effectiveness of antibiotic combinations for initial treatment of central-venous-line infections during total parental nutrition. JPEN J Parenter Enteral Nutr. 2000;24:119-25. DOI: 10.1177/0148607100024002119

192. Sitges-Serra A, Girvent M. Catheter-related bloodstream infections. World J Surg. 1999;23:589-95. DOI: 10.1007/PL00012352

193. Raad I, Hanna HA, Alakech B, Chatzinikolaou I, Johnson MM, Tarrand J. Differential time to positivity: a useful method for diagnosing catheter-related bloodstream infections. Ann Intern Med. 2004;140(1):18-25.

194. Dobbins BM, Catton JA, Kite P, McMahon MJ, Wilcox MH. Each lumen is a potential source of central venous catheter-related bloodstream infection. Crit Care Med. 2003;31:1688-90. DOI: 10.1097/01.CCM.0000063257.04633.9A

195. Raad I, Davis S, Becker M, Hohn D, Houston D, Umphrey J, et al. Low infection rate and long durability of nontunneled silastic catheters: A safe and cost-effective alternative for long-term venous access. Arch Intern Med. 1993;153:1791-6.

196. Mayhall CG. Diagnosis and management of infections of implantable devices used for prolonged venous access. Curr Clin Top Infect Dis. 1992;12:83-110.

197. Hodge D, Punts JW. Diagnosis, prevention, and management of catheter related bloodstream infection during long term parenteral nutrition. Arch Dis Child Fetal Neonatal Ed. 2002;87:F21-4. DOI: 10.1136/hf.87.1.F21

198. Sherertz RJ, Heard SO, Raad II. Diagnosis of triple-lumen catheter infection: comparison of roll plate, sonication, and flushing methodologies. J Clin Microbiol. 1997;35(3):641-6.

199. Fidalgo S, Vázquez F, Mendoza MC, Pérez F, Méndez FJ. Bacteremia due to Staphylococcus epidermidis: microbiologic, epidemiologic, clinical, and prognostic features. Rev Infect Dis. 1990;12(3):520-28.

200. Pollack PF, Kadden M, Byrne WJ, Fonkalsrud EW, Ament ME. One hundred patient years' experience with the Broviac silastic catheter for central venous nutrition. JPEN J Parenter Enteral Nutr. 1981;5:32-6. DOI: 10.1177/0148607181000500132

201. Raad I, Narro J, Khan A, Tarrand J, Vartivarian S, Bodey GP. Serious complications of vascular catheter-related Staphylococcus aureus bacteremia in cancer patients. Eur J Clin Microbiol Infect Dis. 1992;11:675-82. DOI: 10.1007/BF01989970

202. Raad I, Davis S, Khan A, Tarrand J, Etting L, Bodey GP. Impact of central venous catheter removal on the recurrence of catheter-related coagulase-negative staphylococcal bacteremia. Infect Control Hosp Epidemiol. 1992;14(3):215-21.

203. Malanoski GJ, Samore MH, Pefanis A, Karchmer AW. Phlebitis prophylaxis in patients with central venous catheters: A randomized trial. Intensive Care Med. 1993;19(1):34-8. DOI: 10.1007/BF01989970

204. Krzywda EA, Gotoff R, Andris DA, Marciniak TF, Edmiston D, Quebbeman E. Antibiotic lock treatment (ALT): impact on catheter salvage and cost savings. In: Program and Abstracts of the 35th Interscience Conference of Antimicrobial Agents and Chemotherapy; San Francisco, California; 1995.

205. Krzywda EA, Gotoff R, Andris DA, Marciniak TF, Edmiston D, Quebbeman E. Antibiotic lock treatment (ALT): impact on catheter salvage and cost savings. In: Program and Abstracts of the 35th Interscience Conference of Antimicrobial Agents and Chemotherapy; San Francisco, California; 1995.

206. Capdevila J, Segarra A, Planes A, Gasser I, Gavalda J, Pahissa A. Long-term follow-up of patients with catheter-related sepsis (CRS) treated without catheter removal. In: Program and Abstracts of the 35th Interscience Conference of Antimicrobial Agents and Chemotherapy; San Francisco, California; 1995.

207. Stringer WD, Helgerson RB, Maki DG. Candida septic thrombosis of the great central veins associated with central catheters. Critical Care Medicine of the Society of Critical Care Medicine in adult patients; Task Force of the American College of Critical Care Medicine; 1992;10:110-111. DOI: 10.1016/S0001-2443(05)80211-X

208. Raviglione MC, Battan R, Pablos-Mendez A, Aceves-Casillas P, Mullen MP, Taranta A. Infections associated with Hickman catheters in patients with acquired immunodeficiency syndrome. Am J Med. 1989;86:780-6. DOI: 10.1016/0002-9343(89)90473-7

209. Dugdale DC, Ramsey PG. Staphylococcus aureus bacteremia in patients with Hickman catheters. Am J Med. 1990;89:137-41. DOI: 10.1016/0002-9343(90)90299-T

210. Lecciones JA, Lee JW, Navarro EE, Witebsky FG, Marshall D, Steinberg SM, Pizzo PA, Walsh TJ. Vascular catheter-associated fungemia in patients with cancer: analysis of 155 episodes. Clin Infect Dis. 1992;14(4):875-83.

211. O'Grady NP, Barie PS, Bartlett JG, Bleck T, Garvey G, Jorgif M, et al. Practice parameters for evaluating new fever in critically ill adult patients; Task Force of the American College of Critical Care Medicine of the Society of Critical Care Medicine in collaboration with the Infectious Disease Society of America. Crit Care Med. 1998;26:392-408. DOI: 10.1097/00000324-199802000-00046

212. Messing B, Peitra-Cohen S, Deubre A, Bellah M, Bernier JJ. Antibiotic-lock technique: a new approach to optimal therapy for catheter-related sepsis in home-parenteral nutrition patients. JPEN J Parenter Enteral Nutr. 1988;12:185-9. DOI: 10.1177/0148607188012002185

213. Andris DA, Krzywda EA, Edmiston CE, Krepel CJ, Gohr CM. Elimination of intraluminal colonization by antibiotic lock technique. Infect Control Hosp Epidemiol. 1995;16(10):596-8.
231. Gugenbichler JP, Berchtold D, Allerberger F, Bonatti H, Hager J, Pfaffer W, et al. In vitro and in vivo effect of antibiotics on catheters colonized by staphylococci. Eur J Clin Microbiol Infect Dis. 1992;11:408-15. DOI: 10.1007/BF01961855

232. Isaacs JW, Millikan WJ, Stackhouse J, Hersh T, Rudman D. Parenteral nutrition of adults with a 900 milimolal solution via peripheral veins. Am J Clin Nutr. 1977;30(4):552-9.

233. Acra SA, Rollins C. Principles and guidelines for parenteral nutrition in children. Pediatr Ann. 1999;28(2):113-20.

234. Kane MF, Cologniovanni L, McKiernan J, Panos MZ, Ayres RC, Langman MJ, et al. High osmolarity feedings do not increase the incidence of thrombophlebitis during peripheral i.v. nutrition. JPEN J Parenter Enteral Nutr. 1996;20:194-7. DOI: 10.1177/0148607196020003194

235. Williams N, Wales S, Irving MH. Prolonged peripheral parenteral nutrition with an ultralite cannula and low-osmolality feed. Br J Surg. 1996;83:114-6. DOI: 10.1002/bjs.1800830137

236. Everitt NJ, McMahon MJ. Influence of fine-bore catheter length on infusion thrombophlebitis in peripheral intravenous nutrition: a randomised controlled trial. Ann R Coll Surg Engl. 1997;79(3):221-4.

237. Madan M, Alexander DJ, McMahon MJ. Influence of catheter type on occurrence of thrombophlebitis during peripheral intravenous nutrition. Lancet. 1992;339:101-3. DOI: 10.1016/0140-6736(92)91007-U

238. Hecker JF. Potential for extending survival of peripheral intravenous infusions. BMJ 1992:304:619-24. DOI: 10.1136/bmj.304.6827.619.

239. Everitt NJ, McMahon MJ. Peripheral intravenous nutrition. Nutrition. 1994;10(1):97-101. DOI: 10.1007/BF01866129

240. Kuwahara T, Asanami S, Tamura T, Kubo S. Experimental infusion phlebitis: importance of titratable acidity on phlebitic potential of infusion solutions. Clin Nutr. 1996;15:129-32. DOI: 10.1016/S0261-5614(96)80037-9

241. Hessov I, Bojesen-Moeller M. Experimental infusion thrombophlebitis. Importance of the pH of glucose solutions. Eur J Intensive Care Med. 1976;2:97-101. DOI: 10.1007/BF01886129

242. Lai KK. Safety of prolonging peripheral cannula and i v tubing use from 72 hours to 96 hours. Am J Infect Control. 1998;26:66-70. DOI: 10.1016/S0196-6553(98)70063-X

243. Bregenzer T, Conen D, Sakmann P, Widmer AF. Is routine replacement of peripheral intravenous catheters necessary? Arch Intern Med. 1998;158:151-6. DOI: 10.1001/archinte.158.2.151

244. Cornely OA, Bethe U, Pauls R, Waldschmidt D. Peripheral Teflon catheters: factors determining incidence of phlebitis and duration of cannulation. Infect Control Hosp Epidemiol. 2002;23:249-53. DOI: 10.1086/502044

245. Shimandle RB, Johnson D, Baker M, Stottland N, Karrison T, Arnow PM. Safety of peripheral intravenous catheters in children. Infect Control Hosp Epidemiol. 1999;20:73-40. DOI: 10.1086/501574

246. Garland JS, Nelson DJ, Hedges MC. Use of silicon rubber and polyurethane catheters for the delivery of complete intravenous nutrition via a peripheral vein. Clin Nutr. 1993;12:261-5. DOI: 10.1016/0261-5614(93)90043-4

247. Kohlhardt SR, Smith RC, Wright CR, Susic KA. Fine-bore peripheral catheters versus central venous catheters for delivery of intravenous nutrition. Nutrition. 1992;8(6):412-7.

248. Bregenzer T, Conen D, Sakmann P, Widmer AF. Is routine replacement of peripheral intravenous catheters necessary? Arch Intern Med. 1998;158:151-6. DOI: 10.1001/archinte.158.2.151

249. Kuwahara T, Asanami S, Tamura T, Kubo S. Experimental infusion phlebitis: importance of titratable acidity on phlebitic potential of infusion solutions. Clin Nutr. 1996;15:129-32. DOI: 10.1016/S0261-5614(96)80037-9

250. Hessov I, Bojesen-Moeller M. Experimental infusion thrombophlebitis. Importance of the pH of glucose solutions. Eur J Intensive Care Med. 1976;2:97-101. DOI: 10.1007/BF01886129

251. Lai KK. Safety of prolonging peripheral cannula and i v tubing use from 72 hours to 96 hours. Am J Infect Control. 1998;26:66-70. DOI: 10.1016/S0196-6553(98)70063-X

252. Bregenzer T, Conen D, Sakmann P, Widmer AF. Is routine replacement of peripheral intravenous catheters necessary? Arch Intern Med. 1998;158:151-6. DOI: 10.1001/archinte.158.2.151

253. Cornely OA, Bethe U, Pauls R, Waldschmidt D. Peripheral Teflon catheters: factors determining incidence of phlebitis and duration of cannulation. Infect Control Hosp Epidemiol. 2002;23:249-53. DOI: 10.1086/502044

254. Shimandle RB, Johnson D, Baker M, Stottland N, Karrison T, Arnow PM. Safety of peripheral intravenous catheters in children. Infect Control Hosp Epidemiol. 1999;20:73-40. DOI: 10.1086/501574

255. Garland JS, Nelson DJ, Hedges MC. Use of silicon rubber and polyurethane catheters for the delivery of complete intravenous nutrition via a peripheral vein. Clin Nutr. 1993;12:261-5. DOI: 10.1016/0261-5614(93)90043-4

256. Kohlhardt SR, Smith RC, Wright CR, Susic KA. Fine-bore peripheral catheters versus central venous catheters for delivery of intravenous nutrition. Nutrition. 1992;8(6):412-7.

257. Everitt NJ, Madan M, Alexander DJ, McMahon MJ. Fine bore silicone rubber and polyurethane catheters for the delivery of complete intravenous nutrition via a peripheral vein, Clin Nutr. 1993;12:261-5. DOI: 10.1016/0261-5614(93)90043-4

258. Kohlhardt SR, Smith RC, Wright CR, Susic KA. Fine-bore peripheral catheters versus central venous catheters for delivery of intravenous nutrition. Nutrition. 1992;8(6):412-7.

259. Everitt NJ, Madan M, Alexander DJ, McMahon MJ. Fine bore silicone rubber and polyurethane catheters for the delivery of complete intravenous nutrition via a peripheral vein, Clin Nutr. 1993;12:261-5. DOI: 10.1016/0261-5614(93)90043-4

260. Timmer JG, Schipper HG. Peripheral venous nutrition: the equal relevance of volume load and osmolality in relation to phlebitis. Clin Nutr. 1991;10:71-5. DOI: 10.1016/0261-5614(91)90090-Y

261. Kuwahara T, Asanami S, Tamura T, Kanda S. Effects of pH and osmolality on phlebitic potential of infusion solutions for peripheral parenteral nutrition. J Toxicol Sci. 1998;23(1):1-77.

262. Kuwahara T, Asanami S, Kubo S. Experimental infusion phlebitis: tolerance osmolality of peripheral venous endothelial cells. Nutrition. 1998;14:496-501. DOI: 10.1016/S0899-9007(98)00037-9

263. Gazitza R, Wilson K, Bistrian BR, Blackburn GL. Factors determining peripheral vein tolerance to amino acid infusions. Arch Surg. 1979;114:897-900.
