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 suffizienten zentralvenösen Zugangsweg angewiesen, wobei für eine PE <3 Wochen perkutan eingelegte Katheter und für eine PE >3 Wochen subkutan tunnelierte Katheter oder implantierte Portsysteme zur Anwendung kommen. Der zentralvenöse Katheter (ZVK) sollte vor und nach der PE-Applikation und bei ZVK-Okklusion mit physiologischer 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 Infektionsrisikos sollten Blutentnahmen aus dem ZVK vermieden werden. Bei Verdacht auf Katheterinfektion sollten gleichzeitig Blutkulturen peripher und aus jedem Katheterlumen entnommen werden. Bei ausgeprägten lokalen Infektzeichen der Insertionsstelle und klinischem Verdacht auf Katheter-induzierte Blutstrom-Infektion ist die ZVK-Neuanlage vorzunehmen. Im Falle einer kurzzeitig indizierten PE (max. 7–10 Tage) kann eine periphervenöse Zufuhr durchgeführt werden, wenn keine hyperosmolaren Lösungen (>800

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mosm/l) und keine Lösungen mit einer hohen Titrationsazidität bzw. -alkalität (Bikarbonat, Trispuffer) appliziert werden. Die periphere Kanüle (PVK) kann so lange liegen bleiben, wie sie benötigt wird, wenn an der Einstichstelle keine Entzündungszeichen auftreten.

Schlüsselwörter: intravenöse Zugänge, zentralvenöse Katheter, Handhabung zentraler Katheter, katheterassoziierte Infekte, In-line-Filter

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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 Seldinger 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 three 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, subclavian catheters are associated with an increased risk of pneumothorax 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 thromboses, 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 (especially 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 multilumen 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 asepis 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 tunnelled 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 septicaemia [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.

Occlusions 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 RTPase (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 CVC 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-

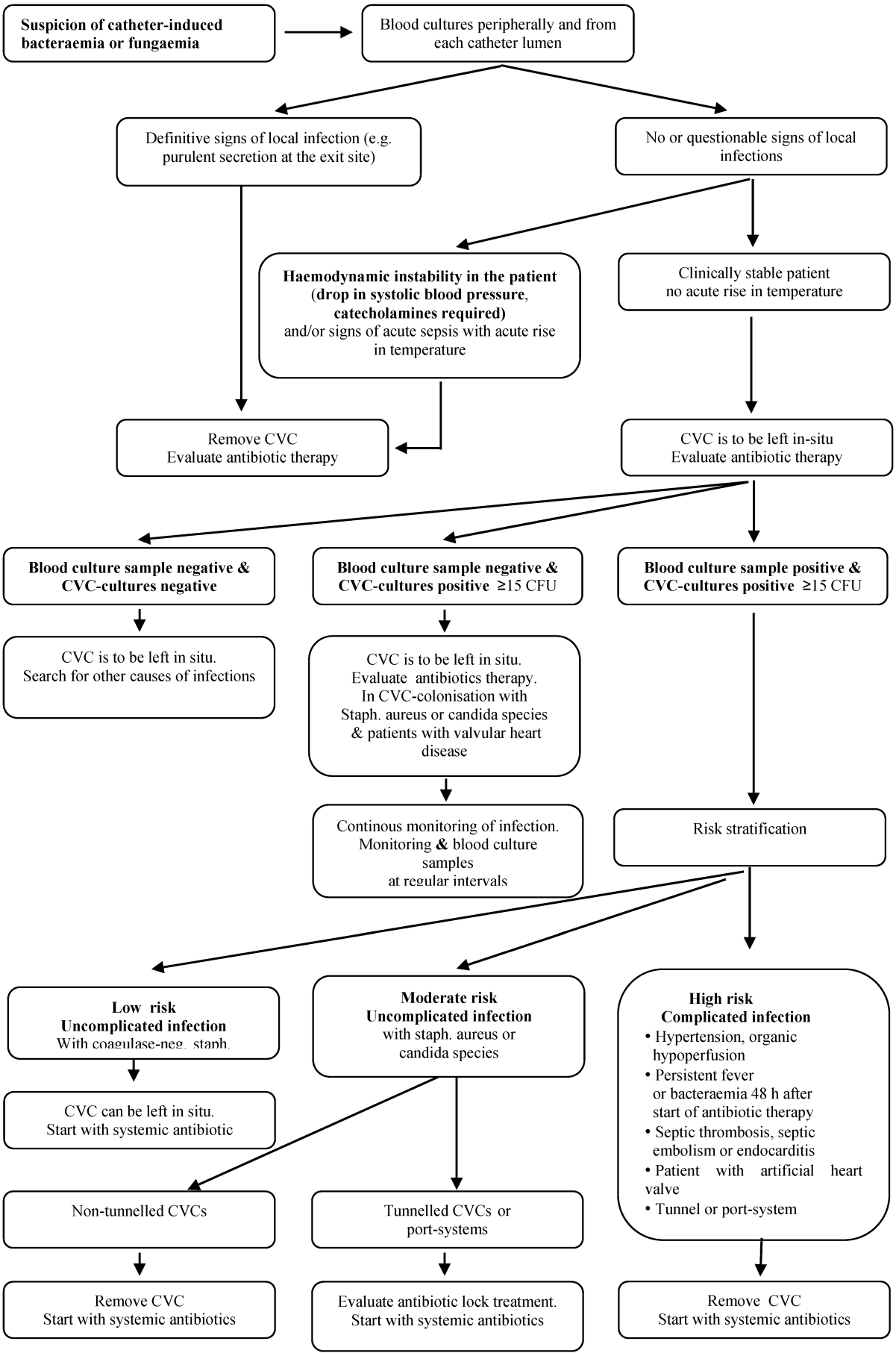

Figure 1: Procedure in case of suspected central venous catheter related systemic infection

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 tunnelled 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 tunnelled 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 mosm/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 mosm/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.

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Please cite as
Jauch KW, Schregel W, Stanga Z, Bischoff SC, Braß P, Hartl W, Muehlebach S, Pscheidl E, Thul P, Volk O, Working group for developing the guidelines for parenteral nutrition of The German Association for Nutritional Medicine. Access technique and its problems in parenteral nutrition – Guidelines on Parenteral Nutrition, Chapter 9. GMS Ger Med Sci. 2009;7:Doc19.

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http://www.egms.de/en/gms/2009-7/000078.shtml

Received: *2009-01-14*
Published: *2009-11-18*