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Intravascular catheter-related infection – current concepts

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Intravascular devices are an integral component of modern-day medical practice. They are used to administer intravenous fluids, medications, blood products and parenteral nutrition. In addition they serve as a valuable monitor of the haemodynamic status of critically ill patients.

Over the past 2 decades the focus of research and development in this field has been the physicochemical properties of catheters, looking at such aspects as improved catheter materials, tensile strength, rupture resistance, biocompatibility and the creation of catheter micro-environments hostile to invading organisms.

Intravascular devices have represented a major advance in terms of patient comfort and care, but with them has come the burden of complications, including a variety of local and systemic infectious complications. In general, intravascular devices can be divided into those used for short-term (temporary) vascular access and those used for long-term (indwelling) vascular access. Long-term intravascular devices usually require surgical insertion while short-term devices can be inserted percutaneously. The main focus of this review and guideline is on short-term catheters.

Magnitude of the problem

Catheter-related infections (CRIs) remain among the top three causes of hospital-acquired infections, with a mortality of up to 25%, and result in prolonged hospitalisation and increased medical costs.[1-6] Central venous catheters (CVCs) account for an estimated 90% of all catheter-related bloodstream infections (CRBSIs).[7] Reported rates of bloodstream infection range from 4 to ≥ 30 per 1 000 central catheter days.[8]

Given the magnitude and seriousness of the problem of CRI, it is essential for health care workers involved with catheter use to have a clear understanding of the diagnosis, pathogenesis, prevention and treatment of this problem and of new developments in the field. Most of these infections can be reversed with appropriate diagnosis and treatment, and many can be prevented.

The findings of the International Nosocomial Infection Consortium (INICC) study, which has just been completed, show that this topic is of particular relevance to practice in our geographical area. This study evaluated device-associated infections in 55 intensive care units (ICUs) in the USA and eight developing countries. There was a substantially significant difference in the number of central venous catheter-associated bloodstream infections in so-called developing countries compared with units in the USA (approximately four times higher). This study has been submitted for publication by the workers involved.[9]

Guidelines for the management of nosocomial infections in South Africa, which include intravascular infections, have recently been published.[10-12]

Definitions of CRIs

Definitions relating to intravascular CRI have been put forward by various workers, but many have complicated matters and been confusing. In part this has been because definitions used for surveillance and research purposes have differed from those used for clinical diagnosis. The Centers for Disease Control and Prevention have suggested sensible definitions[13] that incorporate both clinical and laboratory evidence of catheter infection. These should be universally used in the definition of intravascular catheter infection and are documented in modified form in Table I.

Pathogenesis of CRIs (Fig. 1)

The skin around the insertion site is the most common portal of entry.[14-16] Following placement, a fibrin sheath develops around the catheter which promotes the adherence of pathogens (biofilm layer). Skin organisms then migrate from the insertion site along the external surface of the catheter to colonise the distal intravascular tip and ultimately cause bloodstream infection.

Contamination of the catheter during its manipulation by medical and nursing personnel is the second most common portal of entry of micro-organisms.[15,17-19] Less common causes include haematogenous dissemination from a distal infectious focus, administration of contaminated infusates, and contaminated transducer kits, disinfectants and infusion lines.[20,21]

Table I. Definitions of CRIs

Catheter colonisation: growth of ≥ 15 colony-forming units (semiquantitative culture) or ≥ 10^3 colony-forming units (quantitative culture) from a proximal or distal catheter segment in the absence of local or systemic infection
Local infection: erythema, tenderness, induration or purulence within 2 cm of the skin insertion site of the catheter
Catheter-related bloodstream infection: isolation of the same organism (i.e. the identical species as per antibiogram) from culture (semiquantitative or quantitative) of a catheter segment and from the blood of a patient with accompanying clinical symptoms and signs of bloodstream infection and no other apparent source of infection

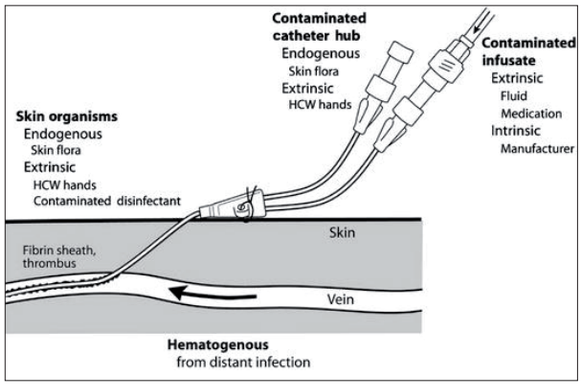

Fig. 1. Pathogenesis of catheter-related infections.

Microbiological profile of CRIs (Table II)

The microbiology of CRI reflects a predominance of skin organisms such as coagulase-negative staphylococci and *Staphylococcus aureus*. Contamination from the hands of medical and nursing personnel is frequently responsible for infection with such organisms as *Pseudomonas aeruginosa*, *Acinetobacter* species, *Stenotrophomonas maltophilia* and *Candida* species.[22-24] Emerging pathogens include species of *Enterococcus*, *Micrococcus*, *Achromobacter*, non-tuberculous mycobacteria and other fungal organisms.[15,22,25,26]

Diagnosis of CRI

Establishing a diagnosis of CRI involves both clinical and laboratory components.

The clinical features are generally nonspecific and include fever, rigors, hypotension and confusion. If there is no apparent source of sepsis in a patient with an intravascular line (especially a CVC) and if the sepsis appears to be refractory to antimicrobial therapy or is of abrupt onset or associated with shock, the possibility of CRI needs to be considered.

Fundoscopy should always form part of the clinical examination, as focal retinal lesions are common in patients with CVC-derived candida infection, even when blood cultures are negative (Fig. 2).

Contamination or purulence at the catheter insertion site is seen in less than half of cases. It is also not predictive of CRBSI with short-term non-cuffed CVCs.[27] The laboratory components include culture of blood and the catheter.

Blood cultures are central to the diagnosis of CRBSI. Two to three 10 ml samples, ideally from separate peripheral venepuncture sites, should be sent to the laboratory.

Paired quantitative cultures, which involve taking blood from both the catheter and a peripheral site, may be particularly useful where luminal colonisation is predominant. The diagnosis is suggested when 5-fold or more colonies are isolated from the blood drawn from the vascular catheter compared with the concurrent peripheral sample.[15,22,23]

The most widely used laboratory technique for culturing the catheter is the semiquantitative roll-plate method.[24] Growth at ≥ 15 colony-forming units from a proximal or distal catheter segment is regarded as significant. Quantitative techniques for culturing the catheter include the sonication and vortexing methods, which involve extracting micro-organisms from the catheter surface into a medium for culturing.[23,28-30]

Newer diagnostic culture techniques include that of the endoluminal brush[31,32] and the Gram stain and acridine-orange leucocyte cytospin (AOLC) test.[33,34]

Table II. Common organisms associated with CRIs

Coagulase-negative staphylococci	*Enterobacter* species
Staphylococcus aureus	*Serratia marcescens*
Candida species	*Citrobacter freundii*
Acinetobacter species	*Enterococcus* species
Pseudomonas aeruginosa	*Bacillus species*
Stenotrophomonas maltophilia	(especially JK strains)
Klebsiella species	

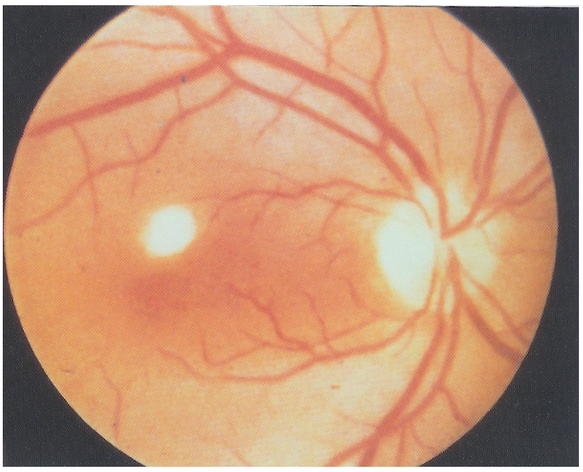

Fig. 2. Candida involving retina.

Use of the endoluminal brush allows samples to be taken via the lumen of the catheter while the catheter remains *in situ*. High sensitivities and specificities have been reported in the diagnosis of CRI with this technique. The technique does not require sacrifice of the catheter, but there is still a delay before culture results are known. There is also a concern that the process of brushing may lead to embolisation of infected biofilm. The place of the endoluminal brush in clinical practice is still to be fully determined.

The Gram stain and AOLC test is a recently described method for rapidly diagnosing CRBSI without catheter removal. The test is performed on blood samples drawn from the CVC and has been reported to have high sensitivities and specificities. The method compares favourably with other diagnostic methods, particularly those that require the removal of the catheter, and may permit early targeted antimicrobial therapy.

Strategies for prevention of CRI

Strict adherence to hand washing and aseptic technique remains the cornerstone of prevention of CRI.

Several other measures have been reported to confer additional protection, some of which need to be considered in the preventive strategy. These include infusion therapy teams, maximal use of barrier precautions during catheter insertion, cutaneous antimicrobials and antiseptics, site of catheter insertion, types of catheter, catheter-site dressings, and luminal antimicrobial flushes and lock solutions.

Infusion therapy team

The presence of an infusion therapy team whose task is to insert and maintain catheters has been shown to decrease the rate of CRBSI by up to 8-fold and limit overall costs.[35,36] Similarly, strict adherence to protocols for catheter insertion in the intensive care unit (ICU), wards and operating theatre are also beneficial in decreasing the rates of CRI.[37,38]

Maximum sterile barriers

Careful hand washing together with the use of sterile gloves, a mask, gown and cap and a large drape have been associated with a more than 6-fold decrease in CVC-related sepsis.[39] The usefulness of this practice cannot be overemphasised.

Cutaneous antimicrobials and antiseptics

Given the important role of cutaneous microflora in the pathogenesis of CRIs, measures to reduce cutaneous colonisation of the insertion site are of vital importance. A three-group trial[40] comparing efficacy of skin decontamination prior to catheter insertion showed that 2% chlorhexidine gluconate was associated with a four-fold decrease in CRBSI compared with 10% povidone-iodine and 70% alcohol.

It is the practice in our unit to use a chlorhexidine gluconate-containing solution for skin preparation.

Tunnelling of CVCs

This involves placing the proximal segment of the catheter under the skin at a distance from the point of entry to the vein. Tunnelling was reported to decrease the rate of CRBSI in one study in critically ill patients.[41] More data are required to support this observation.

Silver-chelated subcutaneous collagen cuffs

These cuffs may be attached to percutaneously inserted CVCs and are designed to act as both a mechanical barrier to the migration of micro-organisms and an antimicrobial deterrent (through the effect of silver ions). They have been shown to lower the risk of catheter colonisation and CRBSI in critically ill patients.[42,43] The anti-infective effect is short-lived, however, as the collagen to which the silver ions are chelated is biodegradable. Other drawbacks include cost and the need for specialised training.

Antiseptic hubs

These have been designed to protect against hub colonisation. Initial work demonstrated a 4-fold decrease in catheter-related sepsis with their use.[44] A major limitation, however, is that protection is only conferred against organism migration along the internal surface of the catheter. They do not protect against the migration of skin organisms along the external surface.

A subsequent randomised trial in 130 catheters failed to show a protective effect.[45]

Dressings

There has been an ongoing debate concerning the best method of catheter dressing. This has essentially revolved around the relative merit of gauze versus transparent films. In a meta-analysis of catheter dressing regimens, CVCs on which a transparent dressing was used were associated with a significantly higher incidence of catheter tip colonisation but a non-significant increase in CRBSI.[46]

A chlorhexidine-impregnated hydrophilic polyurethane foam dressing has been reported to be associated with a reduction in CVC-related infection.[47,48] These antiseptic dressings are affixed about newly inserted catheters, pressed firmly onto the skin and covered with a transparent dressing.

The preference in our unit is to use an adhesive gauze dressing with a central non-adherent pad following prior appropriate administration of a chlorhexidine gluconate-containing solution to the insertion area.

Antimicrobial coating of catheters

In recent years antimicrobial substances have been effectively bonded to catheters in an attempt to limit CRI. Much of this work has pertained to short-term CVCs and will be discussed in further detail later.

Luminal antimicrobial flushes and lock solutions

This practice has been utilised in some units in selected cases with variable success, but it is currently not routinely recommended. Agents that have been used include vancomycin-heparin, minocycline-EDTA and alcohol (25% ethanol).

Treatment principles in CRI

Treatment depends on the stage of infection and the pathogen. As a general rule, if CRBSI is suspected the catheter must be removed and replaced only if necessary.

Most of the infectious complications are self-limiting and resolve after removal of the catheter. Indications for antibiotic therapy include persistent sepsis despite catheter removal, evidence of septic thrombosis of the great veins, clinical or echocardiographic evidence of endocarditis, metastatic foci of infection, underlying valvular heart disease (especially prosthetic valves) and an underlying imunosuppressed state.

In terms of specific pathogens and CRBSI, *S. aureus* and *Candida* species require special mention. In the setting of uncomplicated *S. aureus* CRBSI, the catheter should be removed and at least 2 weeks (and preferably 4 weeks) of parenteral antibiotics given. There is a high relapse rate if antibiotics are given for a shorter time.[49,50]

Systemic antifungal therapy (together with removal of the catheter) should be given in all cases of catheter-related candidaemia in view of the potentially significant sequelae.[51] Amphotericin B and fluconazole (except for fluconazole-resistant organisms such as *Candida glabrata* and *C. krusei*) for at least 14 days have been shown to be equally effective.[52] Newer antifungal agents may also be considered.

Specific catheter types and infection

Specific catheter types that will be reviewed include short peripheral intravenous catheters, peripheral arterial catheters, CVCs, pulmonary artery catheters (PACs) and peripherally inserted CVCs.

Short peripheral intravenous catheters

These remain the most commonly used intravenous device. There is a significant risk of contamination 72 - 96 hours after insertion.[13,53,54] The insertion site should be upper extremity or external jugular vein. A greater risk of infection with lower extremity sites and with cutdowns exists.

Peripheral arterial catheters

These catheters are associated with less infection than PACs, CVCs and short peripheral catheters.[55] This may be explained by high arterial flow around the catheter, which probably decreases the adherence of micro-organisms. It has generally been suggested that these catheters be replaced and relocated no more frequently than every 7 days.[54]

It is our current unit policy to keep peripheral arterial catheters in place for up to 30 days prior to replacement and relocation, unless otherwise indicated.

CVCs

CVCs account for an estimated 90% of all CRBSIs. Non-tunnelled (percutaneously) inserted CVCs are the most commonly used catheters.

A host of risk factors for CVC-related infections have been reported[56-62] including duration of catheterisation, location of the catheter (internal jugular reportedly having a higher rate of CRI than the subclavian vein), the presence of sepsis, type of dressing, multi-lumen catheters (increased frequency of manipulation), less stringent barrier precautious during placement, experience of personnel inserting the device, and administration of parenteral nutrition.

The duration of CVC use has remained controversial. As a consequence, scheduled replacement remains widely practised in many ICUs.[63] The duration of catheterisation has been shown to be a risk factor

for infection in several studies.[56-60,62] Despite the controversy, no catheter should be left in place longer than absolutely necessary. Over the past few years, antimicrobial-impregnated catheters have been introduced in an attempt to limit CRI and increase the time that CVCs can safely be left in place. These include chlorhexidine/silver sulphadiazine- and minocycline/rifampicin-impregnated catheters. Several studies have shown potential benefits of such catheters in terms of reduction of catheter colonisation as well as CRBSI. A recent meta-analysis concluded that chlorhexidine-silver sulfadiazine CVCs appear to be effective in reducing CRI.[64]

Recently published guidelines have, however, been vague and nonspecific with regard to the role of antimicrobial-impregnated catheters and when they should be considered for use. A further concern about the use of these catheters relates to the possible development of antimicrobial resistance, and if they are used a continued surveillance for resistance is required.

A recently completed randomised prospective double-blind study in our multidisciplinary ICU spanning approximately 35 000 catheter hours has addressed many of these issues.[65] This study compared a 14-day placement of standard triple-lumen versus antimicrobial-impregnated CVCs on the rates of CRI. The study demonstrated no difference in CRI rates between the two types of catheter, and indicated that standard CVCs could safely be left in place for 14 days (together with appropriate infection control measures). In this study, the use of parenteral nutrition was not noted to be a risk factor for CRI and there was no difference in infection related to catheter insertion site (internal jugular versus subclavian vein).

We believe that this study has shed some light on previously unanswered questions and controversial areas, and offers suitable direction. On the basis of these results it is our practice to keep standard CVCs in place for 14 days, unless there is an indication for earlier removal. This practice is combined with a stringent protocol relating to aseptic insertion technique and maintenance of the catheter. This protocol is shown in Table III.[37,38]

PACs

Varying rates of infection have been reported with PACs (Swan-Ganz catheters), but most are similar to CVCs. Higher rates have been attributed to the number of manipulations performed. The 'Hands-Off Catheter', which is enclosed in a contamination-proof shield enabling the doctor to prepare, test and insert it without exposure to external contamination, has been associated with a decrease in systemic infection.[66] Most PACs are heparin-bonded, which reduces catheter thrombosis and microbial adherence.[67] These catheters may be left in place for up to 7 days if necessary,[38,54] by which time the patient frequently no longer requires this form of catheter.

With the increasing popularity of non-invasive haemodynamic monitoring devices, PACs are being used less frequently.

Peripherally inserted central venous catheters (PICCs)

PICCs provide an alternative to subclavian or jugular vein catheterisation and are inserted into the superior vena cava or right atrium via the cephalic and basilar veins of the antecubital fossa.

Compared with other CVCs they have traditionally been associated with few mechanical complications, an apparent lower rate of infection, and decreased cost.[68,69] However, recent work has demonstrated that PICCs

Table III. Protocol for insertion and maintenance of central venous catheters

- Clean the skin around the insertion site over a wide area by rubbing for 2 minutes with sterile gauze or cotton wool soaked in a chlorhexidine gluconate-containing solution. Sterile gloves must be worn.
- The doctor, wearing a mask and cap, scrubs up (using a chlorhexidine gluconate-containing scrub solution) and then dons a sterile gown and gloves.
- The doctor then cleans the area again and drapes widely to include the patient's head, neck, chest, limbs and torso down to the pelvis. Only the portion necessary for catheter insertion should be left exposed.
- The 'flush' (heparin 1 000 IU in 19 ml sterile saline) is drawn up, avoiding any contamination by the doctor after cleansing of the stopper on the heparin container. The doctor draws up the 'flush' with a sterile syringe and needle, while the assistant holds the vials.
- Once the line has been inserted, a sterile piece of gauze soaked in a chlorhexidine gluconate-containing solution is applied over the insertion site and adjacent area for approximately 30 seconds.
- The area is then dried with sterile gauze and an adhesive gauze dressing with a central non-adherent pad applied.
- The dressings are changed daily and the insertion site inspected and cleaned in a sterile fashion. Cleaning includes removal of old blood, clots, exudates and crusts and the application of a chlorhexidine gluconate-soaked piece of sterile gauze to the insertion site for approximately 30 seconds, before drying and dressing the area.
- Any signs of local infection (red, hot, swollen, painful, purulence) must be reported.

are associated with a rate of CRBSIs similar to that of conventional CVCs placed in the internal jugular or subclavian veins.[70]

Guidewire exchanges

A recent meta-analysis of CVC replacement strategies revealed that guidewire exchanges were associated with greater risk of CRI but fewer mechanical complications than new-site replacement.[71] If guidewire exchange is used, meticulous aseptic technique is necessary. The procedure should not be performed in the setting of confirmed or clinically suspected sepsis.

In our unit we do not practise guidewire exchanges.

Recommendations regarding the insertion, maintenance and use of intravascular devices[38]

On the basis of current data (including our own), available guidelines and the cumulative anecdotal experience in our unit, both nursing and medical, we have formulated a dedicated policy regarding the insertion, maintenance and use of intravascular devices in the ICU and found it to be favourable.

The basic principle revolves around *strict adherence* to aseptic technique at all times (insertion, maintenance, use).

Recommendations for replacement of intravascular catheters are as follows:

- Standard central venous and acute haemodialysis catheters after 14 days
- Peripheral venous catheters after 3 - 4 days
- Arterial lines after 30 days unless removal is indicated beforehand.

Additional recommendations to limit infection[38]

- Lines used for the administration of blood products must be replaced within 24 hours.
- Lipid-containing parenteral nutrition solutions should be completed within a 24-hour period.
- Parenteral nutrition must be administered via a single dedicated port with the administration line being replaced at 24-hour intervals (performed as a sterile procedure).
- Administration sets such as those used for the delivery of inotropes and antibiotics should be replaced at 72-hour intervals, or before if clinically indicated.
- The day on which lines are changed should be clearly noted on the ICU chart or in the medical records.
- Bridges and their attached lines, transducers and continuous flush devices can be replaced at 7-day intervals, provided there is strict adherence to aseptic technique.
- Aseptic technique also extends to care of ports and caps attached to intravascular devices and includes the spraying of a chlorhexidine gluconate-containing solution following manipulations.

Conclusion

Intravascular CRI remains a major problem. Despite several new technologies and advances, stringent adherence to aseptic technique and infection control measures remain the cornerstone of prevention.

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