# INTRAVASCULAR CATHETER SEPSIS

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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.

## BACKGROUND AND HISTORY

Only a century ago, no means of vascular access existed for the life-sustaining support of critically ill patients. In the late 1800s steel needles became available, and with the advancing knowledge of electrolyte physiology the therapeutic use of intravenous fluid became established. In 1945, following the advent of penicillin and the need for multiple intravenous injections, plastic catheters for continuous vascular access were described.[1,2] A further technological advance took place in 1967 when the placement of long nylon catheters into central veins, to limit medication-associated phlebitis, was described in oncology patients.[3] These catheters were initially inserted by peripheral cutdown techniques and later via percutaneous approaches into the subclavian and jugular veins. Over the past 15 years the focus of research and development has been on the physicochemical properties of catheters, looking at such aspects as improved catheter materials, tensile strength, rupture resistance, biocompatibility and the creation of catheter microenvironments hostile to invading organisms.

Intravascular devices have therefore been 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 relates to short-term catheters.

## MAGNITUDE OF THE PROBLEM

Although no specific local statistics are available, more than 150 million intravascular devices are currently purchased annually by clinics and hospitals in the USA.[4] This includes more than 5 million central venous and pulmonary artery catheters.

Catheter-related infections (CRI) remain among the top three causes of hospital-acquired infections, with a mortality of up to 25%, and result in prolonged hospitalisation (mean of 7 days) and increased medical costs.[5-10] The estimated cost of treating one episode of catheter-related bloodstream infection (CRBSI) in the USA ranged from $8 000 in 1988 to more than $28 000 for intensive care patients in 1994. On the basis of these figures, the economic burden from CRBSI is substantial.

Central venous catheters (CVCs) account for an estimated 90% of all CRBSI.[11] Rates of bloodstream infection range from 4 to 13 per 1 000 central catheter days,[12] with lower rates in respiratory intensive care units and higher rates in burns units.

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

## FORMS OF CATHETER SEPSIS

### Definitions

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

**Table I. Definitions for catheter-related infections**

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| **Catheter colonisation**: growth of ≥ 15 colony-forming units (semi-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 (semi-quantitative or quantitative) of a catheter segment and from the blood (preferably drawn from a peripheral vein) of a patient with accompanying clinical symptoms and signs of bloodstream infection and no other apparent source of sepsis |

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## Pathogenesis of catheter-related infections

The skin around the insertion site is the most common portal of entry.[14-16] The current understanding is that a fibrin sheath develops around the catheter which promotes the adherence of pathogens. This is referred to as the biofilm layer. Skin organisms then migrate from the skin insertion site along the external surface of the catheter to colonise the distal intravascular tip and ultimately cause bloodstream infection. Contamination of the catheter hub during its manipulation by medical and nursing personnel is the second most common portal of entry of micro-organisms. These organisms migrate along the internal surface of the catheter, leading to luminal colonisation and thence to bloodstream infection.[15,17-19] Although much less common than either of the above two mechanisms, haematogenous dissemination from a distal infectious focus or administration of contaminated infusate may also cause CRI.[20,21] Other sources such as contaminated transducer kits, disinfectants and infusion lines are also rare causes.

## Microbiological profile of catheter-related infections (Table II)

The microbiology of CRI reflects a predominance of skin organisms such as *Staphylococcus epidermidis*, *S. aureus*, *Bacillus* species and *Corynebacterium* species (especially JK strains). JK bacteraemia occurs almost exclusively in severely immunosuppressed patients who are or have been receiving broad-spectrum antibiotics and who have indwelling intravascular devices.

**Table II. Common organisms associated with catheter-related infections**

| | |
|---|---|
| *Staphylococcus epidermidis* | *Enterobacter* species |
| *S. aureus* | *Serratia marcescens* |
| *Candida* species | *Citrobacter freundii* |
| *Acinetobacter* species | *Enterococcus* species |
| *Pseudomonas aeruginosa* | *Bacillus* species |
| *Stenotrophomonas maltophilia* | *Corynebacterium* (especially JK strains) |
| *Klebsiella* species | |

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.[4,22-24]

Emerging pathogens, including species of *Enterococcus*, *Micrococcus* and *Achromobacter*, rapidly growing mycobacteria such as *Mycobacterium fortuitum* and *M. chelonei*, and fungal organisms such as *Malassezia furfur*, *Rhodotorula* species, *Fusarium* species, *Trichosporin* species and *Hansenula anomala* have also caused catheter infections.[15,22,25,26]

## Diagnosis of catheter-related sepsis

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 central venous catheter) and if the sepsis appears to be refractory to antimicrobial therapy or is of abrupt onset and associated with shock, the possibility of line-related sepsis 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. Inflammation or purulence at the catheter insertion site is seen in less than half the cases.

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 venipuncture 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 fivefold or more colonies are isolated from the blood drawn from the vascular catheter as 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] In this method, cultures are obtained from a segment of the catheter after it has been removed from the patient by rolling the catheter segment across the surface of a blood-agar plate at least four times and then determining the number of colonies present after a period of incubation. Growth of $\geq 15$ 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. This entails either flushing out the catheter segment and immersion in culture medium or placement of the segment in culture medium with sonication.[23,27,28] Quantitative culture is the most sensitive technique for diagnosis of catheter-related infection. Other techniques such as Gram staining of the catheter surface and culture of the tip in broth are associated with high false-positive rates. A newer diagnostic culture technique is that of the endoluminal brush. This allows samples to be taken via the lumen of the catheter with a brush while the catheter remains *in situ*. A sensitivity of 95% and a specificity of 84% in the diagnosis of CRI has been reported with this technique.[29,30] This technique does not require sacrifice of the catheter, but there is still a delay before culture results are known. There are also concerns 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 determined.

## PREVENTIVE STRATEGIES FOR CRI

*Strict adherence to handwashing and aseptic technique remains the cornerstone of prevention of CRI.* However, other measures may confer additional protection and need to be considered in the preventive strategy. These include infusion therapy teams, use of barrier precautions during catheter insertion, cutaneous antimicrobials and antiseptics, site of catheter insertion, tunnelling of CVCs, silver-chelated subcutaneous collagen cuffs, antiseptic hubs, catheter-site dressings and the use of antimicrobial impregnated catheters.

### Infusion therapy team

The presence of an experienced infusion therapy team whose task is to insert and maintain catheters has been shown to decrease the rate of CRBSI up to eightfold and limit overall costs.[31,32] Similarly, strict adherence to protocols for catheter insertion in the intensive care unit (ICU) and theatre are also beneficial in decreasing the rates of CRI.

### Maximum sterile barriers

Careful handwashing together with the use of sterile gloves, a mask, gown and cap and a large drape have been associated with a greater than sixfold decrease in CVC-related sepsis[33] and a fourfold decrease in the rate of bacteraemia related to pulmonary artery catheters.[14] The use of this practice cannot be over-emphasised.

### Cutaneous antimicrobials and antiseptics

Given the important role of cutaneous microflora in the pathogenesis of catheter-related infections, measures to reduce cutaneous colonisation of the insertion site are of vital importance.

For skin decontamination before catheter insertion in a three-group trial[34] comparing the efficacy of treatment, 2% chlorhexidine gluconate was associated with a fourfold decrease in CRBSI as compared with 10% povidone-iodine and 70% alcohol. The use of PNB ointment (polymixin-neomycin-bacitracin) at the skin entry site has been associated with a lower rate of CRBSI; however, the overall protective effect is offset by a higher risk of fungal colonisation and infection.[35]

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. A lower rate of CRBSI has been reported in one study in critically ill patients.[36] 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.[37,38] 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. A fourfold decrease in catheter-related sepsis has been demonstrated with their use.[39] 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.

### Dressings

There has been ongoing debate concerning the best method of catheter dressing. This has essentially revolved around the relative merit of gauze and tape dressings 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.[40]

The preference in our unit is an adhesive gauze dressing with a central non-adherent pad.

### Antimicrobial coating of catheters

In recent years, antimicrobial substances have been effectively bonded to catheters, especially those designed for short-term use. Two coated CVCs are currently available, a chlorhexidine/silver sulphadiazine catheter and a minocycline/rifampicin catheter. Several studies have shown potential benefits of such catheters in terms of reduction of catheter colonisation as well as CRBSI.[16,41-43]

A potential drawback of the chlorhexidine/silver sulphadiazine catheter, however, is that the coating is applied only to the external surfaces and does not protect against endoluminal colonisation as a result of hub contamination. The minocycline/rifampicin catheter is coated on both the external and internal surfaces and may therefore be more effective.[44] One of the concerns about the use of antimicrobial-impregnated catheters relates to the possible development of antimicrobial resistance, and where they are used continued surveillance for resistance is required.

## TREATMENT PRINCIPLES OF CATHETER-RELATED INFECTION

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-limited 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 immunosuppressed 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 2 weeks of parenteral antibiotics given. There is a high relapse rate if these are given for a shorter time.[45,46]

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.[47] Amphotericin B or fluconazole (except for fluconazole-resistant organisms such as *Candida glabrata* and *C. krusei*) should be commenced. Fluconazole 400 mg daily for at least 14 days has been shown to be as effective as amphotericin B 0.5 mg/kg/d for 14 days, with fluconazole being less toxic.[48]

## SPECIFIC CATHETER TYPES AND INFECTION

### Short peripheral intravenous catheters

These remain the most commonly used intravascular devices. There is a significant risk of contamination 72 hours after insertion.[49] The insertion site should be an upper extremity or the external jugular vein. There is a greater risk of infection with lower extremity sites and with cutdowns.

### Peripheral arterial catheters

Peripheral arterial catheters are associated with less infection than pulmonary artery catheters (PACs), CVCs and short peripheral catheters.[50] This may be explained by high arterial flow around the catheter, which probably decreases the adherence of micro-organisms.[51] The Centers for Disease Control and Prevention guideline[13] suggests that replacement of catheters and relocation of insertion sites need take place no more frequently than every 4 days.

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

### Central venous catheters

CVCs account for an estimated 90% of all CRBSI. Non-tunnelled (percutaneously) inserted CVCs are the most commonly used central catheters. A host of risk factors for CVC-related infections have been reported, including duration of catheterisation, location of the catheter (the internal jugular 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 precautions during placement, experience of personnel inserting the device, and the administration of parenteral nutrition.

The duration of CVC use remains controversial. Despite this, however, no catheter should be left in place longer than absolutely necessary. The duration of catheterisation has been shown to be a risk factor for infection in several studies[52-55] and scheduled replacement remains widely practised in most ICUs. In a recently performed study in mainland Britain, where 165 ICUs were surveyed,[56] catheters were routinely replaced, the mean time being 6.5 days.

We have recently completed and analysed a CVC study in the multidisciplinary ICU at Johannesburg Hospital. The study was a prospective randomised double-blind study which entailed comparison of a 14-day placement of standard triple-lumen versus antimicrobial-impregnated (chlorhexidine/silver sulphadiazine) CVCs on the rates of CRI. Our aim was to determine whether we could safely increase the duration of insertion time from 7 days to 14 days and the influence of the antimicrobial-impregnated catheter on the incidence of CRI.

One hundred and eighteen critically ill patients were included in the study, which spanned 34 951.5 catheter hours (1 456 catheter days). Sixty-two patients received a standard catheter and 56 an antimicrobial-impregnated catheter. Eighteen of the patients developed a CRBSI, 1 of whom died, and 5 patients demonstrated catheter colonisation. This rate of CRBSI compares favourably with those previously reported, in which many of the catheters were in place for shorter periods of time than in our study.[12,39]

The most frequent source of infection was the skin, followed by hub and infusate contamination and lastly haematogenous seeding. The sources and organisms were identified with the aid of restriction-fragment length DNA subtyping.

We were unable to show any difference in CRI rates between the two types of catheters in the study. Most importantly we were able to conclude that standard CVCs can safely be left in place for 14 days (with stringent infection control measures). Parenteral nutrition was not noted to be a risk factor for catheter sepsis, and neither was the site of insertion (internal jugular vein versus subclavian vein).

On the basis of the results of this study, it is now our practice to keep standard CVCs in place for 14 days unless there is an

**Table III. Protocol for insertion of central venous catheters**

- Clean the skin around the insertion site over a wide area by rubbing for 2 minutes with sterile gauze or cottonwool 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 manner. 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.

indication for earlier removal. This practice goes hand-in-hand with a stringent protocol relating to aseptic insertion technique and care of the catheter. A modified form of this protocol appears in Table III.

### Pulmonary artery catheters

Varying rates of infection have been reported with PACs (Swan-Ganz catheters), but most are similar to CVCs. Where higher percentages have been reported, this has 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.[57] Most PACs are heparin-bonded, which reduces catheter thrombosis and microbial adherence.[58] The current Centers for Disease Control and Prevention guideline recommends catheter replacement at least every 5 days.[13] It is our current practice to keep in PACs for up to 7 days if necessary, by which time the patient frequently no longer requires this form of catheter.

### 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 are associated with few mechanical complications, an apparent lower rate of infection[59,60] and decreased cost. The length of time that these catheters can be left in place safely has not yet been determined, although they have been used successfully for extended periods.

### 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.[61] If guidewire exchange is used, meticulous aseptic technique is necessary. This procedure should not be performed in the setting of confirmed or clinically suspected sepsis. In our unit we do not practice guidewire exchanges.

## ADDITIONAL RECOMMENDATIONS TO LIMIT INFECTION

On the basis of the results of our study, previous guidelines[13] and the cumulative anecdotal experience in our unit, both nursing and medical, we now have a dedicated policy regarding the insertion, maintenance and use of intravascular devices. The basic principle revolves around *strict adherence* to aseptic technique at all times. It is our present policy to change central venous and haemodialysis catheters after 14 days, peripheral venous catheters after 3 days and arterial lines after 30 days, unless removal is indicated beforehand. 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 are 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.

It is our policy to replace bridges and their attached lines, transducers and continuous flush devices every 7 days. This is longer than the recommended 96-hour interval,[13] but it is our experience that provided there is strict adherence to aseptic technique, the infection risk is not increased. 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 catheter-related sepsis remains a major problem. Stringent adherence to aseptic technique and infection control measures remain the cornerstone of prevention.

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