Infection and central vascular access devices

Central vascular access devices are widely used in the neonatal and paediatric intensive care unit, however, the risk of nosocomial infection is exacerbated with their usage. Catheter-related bloodstream infections continue to contribute to the causes of morbidity and mortality amongst vulnerable populations. National and local infection control policies should be implemented in order to minimise the risk of infections and reduce their potentially devastating effects.

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Key points

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1. The neonatal and paediatric population are subject to a greater risk of infection due to their vulnerability and immature systems.
2. Coagulase negative Staphylococcus is the most prevalent causative pathogen for CR-BSI in the intensive care environment.
3. Vigilance in complying with infection control directives is required when inserting and managing central vascular access devices, to prevent infection.
4. One of the most important aspects of management is to 'scrub the hub' prior to any manipulations.

The use of central vascular access devices (CVADs) in the neonatal and paediatric intensive care unit (NICU/PICU) has become commonplace particularly for the provision of parenteral nutrition. CVADs are also increasingly being used within the home environment for infants and children with complex care needs. This raises issues regarding carer and parental education and competence in managing these devices to ensure the risk of complications associated with their use is minimised. The incidence of catheter-related blood stream infections (CR-BSIs) is reported as 7.7 per 1000 in the paediatric ICU population, 11.3 per 1000 for infants less than 1 kg and 4 per 1000 for infants above 2.5 kg[1,2].

Skin flora are suggested to be the cause of approximately half of all cases of late-onset neonatal sepsis[3]. As most are nosocomial in origin, improving hand washing, complying with no-touch/aseptic technique directives and reducing the number of line manipulations may help to alleviate the incidence of CR-BSIs. Achieving this is crucial as the consequences of CVAD complications are multifactorial and include increased risk of morbidity[4] and mortality[5], increased length of stay within healthcare services[6] and increased costs of caring for patients in all age groups[7].

The aim of this article is to provide an overview of CVAD catheter-related infection as it is the most commonly reported complication[8], while often being the most difficult to treat. The pathogenesis of offending micro-organisms is explored and the strategies currently employed to prevent and reduce early and late-onset infection are evaluated.

Central vascular access devices

Central vascular access devices are essential to provide cardiovascular monitoring, blood sampling, delivery of hypertonic intravenous infusions (IV), medications and nutrition. CVADs can be venous or arterial and may be sited peripherally or surgically. In the neonatal population they are usually placed within the umbilical artery and/or vein in the initial newborn period, if required. For longer term IV therapy, peripherally inserted central lines (PICC) are most commonly used. In older infants and paediatric patients other larger vessels are preferable for example, subclavian, internal jugular and femoral[9]. The complications that can arise from the use of femoral access in neonates has led some clinicians to be cautious of this route. Femoral access has been linked with transient ischaemia of the lower limbs and an increased risk of CR-BSI although it is an acceptable route when no other is available[10].

There are several types of CVADs that can be used. The gauge, type and material the catheter is made from will dictate which would be most appropriate for use in any given situation and manufacturers' recommendations should always be followed. **TABLE 1** provides a list of the main types of CVADs in current use.

These devices provide direct access to the circulation and therefore complications can arise, particularly central catheter-related infections.

Infection rates in NICU and PICU

There are many predisposing factors that make compromised infants and children with CVADs more susceptible to catheter-

Type of central vascular access device	Site	Indications for use
Peripheral intravenous central catheter (PICC)	Peripheral insertion advanced to large central vein eg superior vena cava	Long term access needed Administration of total parenteral nutrition Infusion of inotropic drugs Infusion of non-isotonic fluids eg 15% dextrose Chemotherapy
Umbilical arterial catheter catheter (UAC) Arterial catheter	Umbilical artery commonly positioned between T6 and T10 Radial artery placement Femoral artery placement	Blood sampling for blood gas analysis, serology profiles Infusion of fluids Blood pressure monitoring *NB: Intravenous medication can be contraindicated*
Umbilical venous catheter	Umbilical vein resting in inferior vena cava	Emergency newborn central access Infusion of fluids Exchange transfusion Administration of blood products Administration of intravenous drug therapy
Intraosseous needle	Antero-medial aspect of the tibia or alternatively the anterior aspect of femur, superior iliac crest	Emergency central access Infusion of fluids Administration of blood products Administration of intravenous drug therapy
Tunnelled catheters eg Hickman or Broviac	Jugular vein Subclavian vein – the tip of the catheter should lie in the superior vena cava above the right atrium	Total parenteral nutrition Administration of vesicant – intravenous drugs Chemotherapy Prolonged antibiotic therapy
Totally implantable venous access systems eg Port-a-cath	Usually inserted into the chest or arm	Prolonged need for vascular access Chemotherapy Coagulation factors in haemophillia cases

TABLE 1 Type of central venous access device.

General
■ Immaturity/prematurity
■ Poor skin integrity
■ Maternal infection
■ Prolonged rupture of membrane/prolonged premature rupture of membranes
■ Compromised and or immature immune system leading to an impaired phagocytic response
■ Severity of existing illness
■ Increasing length of stay in NICU/PICU due to increasing survival rates of severely compromised infants and children
Specific to CR-BSI
■ Longer duration of catheter placement
■ Repeated catheter placement
■ Catheter material used
■ Port systems that can form sludge within the reservoir
■ Infusion of total parenteral nutrition

TABLE 2 Pre-disposing risk factors[11].

Term	Definition
Catheter-related bloodstream infection (CR-BSI)	A positive peripheral blood culture with associated colonisation of the catheter hub or tip, with or without the presence of clinical symptoms
Neonatal early-onset infection	Infection diagnosed within 72 hours of birth
Neonatal late-onset (nosocomial) infection	Infection diagnosed after 72 hours of age
Bacteraemia	Viable bacteria in the bloodstream. Diagnosed by positive blood culture
Septicaemia	An ill-defined term that mixes parts of bacteraemia and sepsis together. It is more precise to use the terms bacteraemia or sepsis
CoNS CR-BSI	Two or more blood cultures drawn on different occasions that are positive for coagulase negative Staphyloccoci
Sepsis	Whole body inflammatory response to microbes in the blood. Viable micro-organisms detected in the bloodstream. Diagnosed by positive blood culture concurrent with severe clinical symptoms[17]. Can be caused by bacteraemia, fungaemia or viraemia
Catheter colonisation	Presence of significant growth of microbes on the intra or extra-luminal surface of the catheter beneath the skin. Clinical symptoms are not present.

TABLE 3 Definitions of infections.

related infections (**TABLE 2**).

The onset of infection can be subdivided into two main categories, early and late. Early-onset infections in the neonate are commonly related to maternal vertical transmission, whereas late-onset infections are more commonly nosocomial for all hospitalised age groups or community-acquired, although horizontal transmission via siblings and relatives can also occur. Vascular CR-BSIs are usually nosocomial[6,12,13]. These infections are caused by care received in the hospital environment and are not related to the patient's primary condition. The main pathogens include gram positive, gram negative and fungal infections[14]. The time of onset can influence the rate of recovery and outcome.

There is a lack of consensus among researchers regarding the definitions provided for early and late-onset infection, and confirmed as opposed to suspected infection. In articles where no definitions

are provided making comparisons is problematic as the parameters are unclear. Even when definitions are provided, consistency is sometimes lacking in either the definition or the terminology used, eg the terms bacteraemia, sepsis and septacaemia all being used interchangeably. Therefore **TABLE 3** provides the definitions that will be used within this article.

Infections can arise in a number of ways. The main routes of contamination are shown in **TABLE 4**.

The CVAD catheter hub can be a primary reservoir for micro-organisms, especially in catheters that receive numerous manipulations. This can be multiplied in catheters with more than one lumen, as patients requiring a CVAD with multiple lumens tend to require more intensive interventions. In such compromised patients the risk of infection is greater[7,16]. Contamination of the infusion system can occur inside the lumen of the catheter, outside the catheter but inside the circulatory system, outside the catheter but limited to the surrounding area and lastly, outside the catheter and with microbes dispersing beyond the insertion site. The latter is commonly referred to as a CR-BSI.

Chien et al[17] suggested that bacteraemia associated with CVADs was 13 per 1000 catheter days as opposed to 3 per 1000 days for infants without a CVAD. This study also proposed that the risk of contracting a nosocomial BSI with percutaneous and Broviac catheters was greater than with umbilical venous catheters. The incidence of BSI with Candida is reported as being anywhere between 3 and 24% of all premature infants depending on the gestational age, where the lower the gestation the greater the risk of contracting candidaemia[18].

Common causes	Cross contamination Contamination at time of catheter placement Contamination of insertion site Contamination by host skin flora Contamination of CVAD by healthcare professional Contamination through manipulation of system
Rarer causes	Contamination by migration of bacteria within lumen of catheter Contamination of infusate Secondary contamination from primary infection traversing to catheter (septic seeding[14]).

TABLE 4 CVAD contamination routes, adapted from Krzywda and Edmiston[14] and Kelly[15].

Type of surface	Micro-organisms can adhere to many types of surface. Some surfaces are better able to support certain microbes than others. For example, the charge (+ve or -ve) of a surface will affect how well it can support a particular micro-organism. Additionally, surfaces that can receive nutrients are also more able to support biofilm formation. Whether the surface is rough or smooth can affect the ease with which microbes can adhere
Attachment to surface Reversible	Attachment to a surface by micro-organisms can be reversible or irreversible. Reversible attachment occurs by a variety of routes including the natural motion of the microbes through the lumen within the infusate and sedimentation in slow moving infusates.
Irreversible	Irreversible attachment occurs when microbial cells form cell-to cell bridges that adhere the cells to the surface they are in contact with.
Colonisation by microbes	Colonisation occurs as the micro-organisms adhering to the surface reproduce and begin to form a biofilm.
Detachment of part of biofilm	This is where parts of the biofilm become separated and move away from the primary site. This is also known as dispersion or dissolution and more recent research would suggest that it is an active process regulated by the colony.

TABLE 5 Factors affecting biofilm formation[24].

Pathogenesis

The epidemiology of predominant microbes within intensive care has changed over recent years. In the 1980s the most prevalent pathogen causing catheter-related infections was *Staphylococcus aureus*[7]. In the 1990s this changed to *S. epidermidis* closely followed by Enterococci[7,14]. In recent years Coagulase Negative Staphylococcus (CoNS) has been the dominant cause of late-onset central catheter-related bacteraemia[19]. The most common species in NICU tend to be *S. epidermidis, S. haemolyticus* and *S. warneri*[11].

Bizzaro and colleagues[3] suggested that the incidence of late-onset sepsis had increased while early-onset sepsis had reduced, whereas Stoll and workers[20] found that the overall incidence of early-onset sepsis had remained the same, although the responsible pathogens exhibited a changing pattern.

Resistant strains of micro-organisms are well documented, the most common being methicillin resistant *Staphylococcus aureus* (MRSA). Numbers of MRSA bacteraemia episodes in England, Wales and N. Ireland have been falling in the last couple of years whereas the resistance of *E.coli* is increasing[21]. When infection is present it is imperative to know not only where the infection is located but also if the microbial strain is resistant in order to prescribe the most appropriate and effective therapy. Research by Raimundo and colleagues[11] suggested that resistant strains were identifiable and therefore appropriate treatment could be provided. On a cautionary note, De Giusti and workers[22] found there was a high false positive rate of resistant strains that could lead to the inappropriate use of vancomycin and thus the development of vancomycin-resistant bacteria due to overuse. However the HPA reported in July 2008 that resistance to vancomycin in England, Wales and N. Ireland does not appear to have increased since 2007 in relation to MRSA[21]. Research to explore the development of new antimicrobials is ongoing and as new drugs become available, resistance begins to emerge within a few years of their use[21]. Currently there is a new class of anti-fungals called echinocandins. The effectiveness of this new group within the paediatric and infant populations is presently being studied[23].

The relevance of biofilms

A biofilm can be thought of as a colony of micro-organisms protected by a matrix-like structure. Once a patient has a vascular

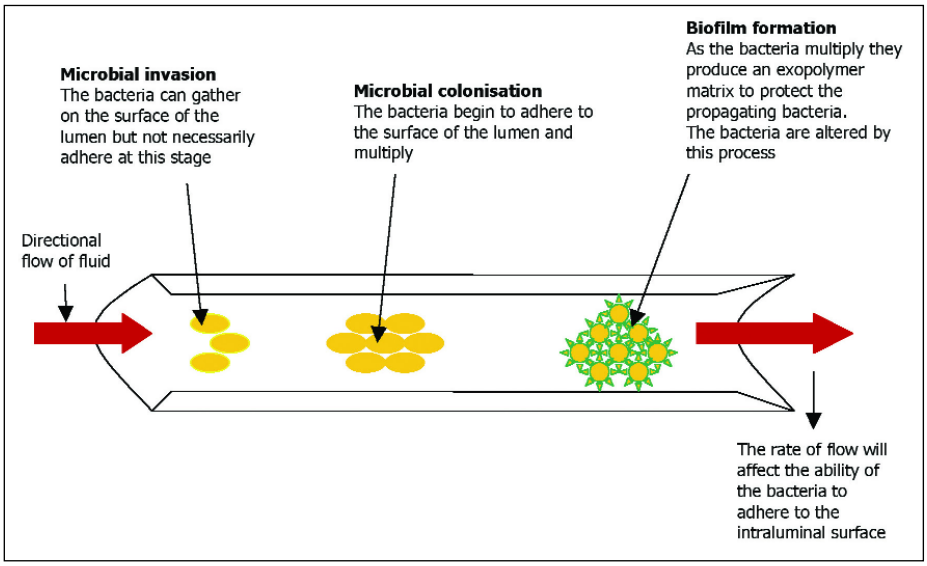

FIGURE 1 Process of microbial biofilm formation.

catheter in place, microbes will begin to irreversibly adhere to the intra-luminal surface of the catheter as conditions allow[24]. The microbes then multiply and a protective layer is produced otherwise known as a biofilm. There is some debate as to the role biofilms have in infections arising from vascular catheters although they are known to be the cause of many bacterial infections[25]. They have also been observed in fungal and yeast infections[23,24]. The development of a biofilm is dependent on a number of factors including the type of surface the microbes are adhering to, the type of micro-organisms trying to form a colony and the flow of any fluid through the lumen of the tube (**FIGURE 1 and TABLE 5**). As separate colonies grow they can merge and eventually this can lead to a narrowing or blocking of the lumen[25]. However, Raimundo and workers[11] found that the most predominant Staphylococcal neonatal infections did not produce a biofilm. This area requires further research to clarify the issue of increased virulence through alternative mechanisms, particularly in the neonate, as this is not clearly understood. In addition, mathematical and experimental models do not always take fluid flow sufficiently into account[25] and this may pose difficulties when attempting to extrapolate the information into practice.

Increased knowledge regarding biofilms is necessary as it is harder for antimicrobial therapy to break through the protective matrix-like layer to disinfect the micro-organisms below. This means that even during treatment the biofilm can continue to grow and it may in part be aiding the development of resistant strains.

Strategies specific to CR-BSI

There have been several developments to combat CVAD-related infections not all of which have been as effective as hoped. Even when efficacy is demonstrated, the concern for many of the developments is that whilst they appear to be useful they could in reality exacerbate the problem of microbe resistance.

Manufacturers have attempted to address the problem of vascular CR-BSIs by developing antimicrobial catheters. These are coated with an antimicrobial, silver compound, antiseptic or a dual coating such as chlorhexidine-silver sulfadiazadine (C-SS) and more recently minocycline-rifampin (M-R). Most antimicrobial-catheter research has been based on fairly short dwell times (<7 days) although one study found no significant benefit from coated catheters when longer dwell times were considered[26]. The epic2 guidelines recommend that antimicrobial-catheters only be used with adults[27] and this may be due to the fact that limited research is available on their use in children[28].

There have been a number of reviews exploring the use of prophylactic antimicrobials including vancomycin and fluconazole to prevent CR-BSIs. Whilst these have all demonstrated a reduction in the number of infections recorded, the authors have also highlighted the potential for emerging resistance over time[29-32].

This has led some researchers to consider whether antimicrobial locks would be as effective without the concerns regarding resistance. A study by Garland et al[33] found that a vancomyin-heparin lock in compromised infants reduced the incidence of vascular CR-BSIs without appearing to promote vancomycin resistance. However, this study also identified that hypoglycaemia was a potential complication and therefore caution should be exercised.

Despite such developments these infections still persist and therefore preventative strategies should continue to be explored and utilised whereever possible. There are two main approaches to vascular catheter management with CR-BSIs. The catheter can either be removed as soon as sepsis is suspected or diagnosed. Alternatively the catheter can be kept *in-situ* whilst treatment for sepsis is instigated. Both approaches have their merits and ideally each incidence of CR-BSI should be treated based on the clinical and laboratory findings of the individual patient.

When fungal infection is suspected/diagnosed, best practice would be to remove a central catheter as this lowers the risk of associated mortality and morbidity[34].

Catheter withdrawal is also usually recommended where bacteraemia has been diagnosed. However, there is a case for not withdrawing the catheter if CoNS is isolated on culture as a good clinical response can be achieved with the appropriate antibiotic therapy[35].

In neonates and children where gaining venous access is extremely difficult, clinicians will usually attempt to salvage the catheter by commencing treatment with vancomycin[36]. Even so, in the presence of persistent positive blood cultures, or if the patient continues to exhibit clinical symptoms of infection with antimicrobial therapy, then the catheter should be removed. Within the paediatric population there has been a small study in the field of oncology investigating whether using hydrochloric acid as an adjunct to antibiotic therapy would enable the catheter to be salvaged. Whilst the results were encouraging further research would be required before this could be recommended in practice[37].

Infection control initiatives and practice

A report by the HPA highlighted the need for further research into MRSA as the incidence is increasing amongst children[38]. There are several new government directives and national initiatives promoting the reduction of healthcare

associated infections (HCAI). A key message from these documents is a more prudent and thoughtful use of antimicrobial therapy to prevent the overuse of broad spectrum antibiotics[27-39]. The standardisation of practices related to the minimisation of HCAIs is one of the most important strategies that can be implemented, as the evidence concludes that aseptic care reduces HCAIs. Conversely, inexperienced healthcare workers (HCWs), who lack the appropriate training in such clinical approaches are more likely to increase HCAIs when maintaining CVADs[7].

The most simple intervention to reduce HCAIs, easily achievable by all, is effective hand-washing at the point of care. Hands, gloves, uniforms and gowns all harbour microbes and are easily transferable by HCWs in the course of their daily work[40,41] when universal precautions are not taken. Hand decontamination contributes greatly to the reduction of cross infection. The five moments for hand hygiene described by the World Health Organisation[42] have been incorporated into the *Clean Hands Saves Lives* alert issued by the National Patient Safety Agency[40]. Despite this continually promoted message, standards remain suboptimal[27] and HCWs must continue to be vigilant when hand washing.

All HCWs must ensure they are familiar with the recommendations proposed by epic2[27], the Health Protection Agency[21], the NPSA[40] and the Department of Health's documents on Employee Uniforms and Workwear, and the Health Act 2006[39,41]. While the nine interventions recommended by epic2 surrounding the prevention of infections associated with the use of CVADs only apply to children aged one year and older, the underlying principles (**TABLE 6**) are just as relevant to the neonatal population.

By incorporating these recommendations into local policies and implementing changes in practice to comply with best evidence, together HCWs, patients and their carers can reduce HCAIs. It is important that all who come into contact with patients and/or patient areas are educated in the prevention of HCAIs including parents, families and visitors.

When a patient is to have a CVAD placed, whether it be a PICC, UAC/UVC, tunnelled catheter or a totally implantable device, the procedure must be a 'no touch' technique with full aseptic precautions including a sterile gown, mask, hat, gloves and large drape/barrier employed[29].

- Education of healthcare workers and patients
- General asepsis
- Selection of catheter type
- Selection of catheter insertion site
- Maximal sterile barrier precautions during catheter insertion
- Cutaneous asepsis
- Catheter and catheter site care
- Catheter replacement strategies
- General principles for catheter management

TABLE 6 epic2 recommend nine interventions[27].

In addition, in an effort to reduce the risk of CVAD-related infections the most appropriate catheter should be chosen. Consideration should be given to the material the catheter is made of, the number of lumens required for effective treatment options, and whether the catheter should be tunnelled or totally implantable[27]. In the UK most short-term catheters are made from polyurethane and long-term tunnelled catheters are made from silicone[27]. It is recommended that a single lumen catheter be the one of choice and multi-lumened catheters only be used when multiple treatment regimes are necessary. In addition, parenteral nutrition should only be given through one dedicated port of a multi-lumened catheter[27]. For patients requiring long-term therapy (>4 weeks) epic2 recommend that a tunnelled or totally implantable device is used[27].

When inserting a CVAD it is important to consider local skin flora present and the risk of thrombophlebitis. Thrombophlebitis or thrombosis can also result from an inappropriate type of VAD causing intraluminal damage to the wall of the vein[43]. Skin preparation at the site of insertion is also important. Current national guidelines recommended the use of a 2% chlorhexidine gluconate in 70% isopropyl alcohol solution[27]. However an aqueous solution of chlorhexidine is preferable in neonates due to the potential toxicity of alcohol-based skin preparations via percutaneous absorption. In paediatrics, where chlorhexidine sensitivity is an issue, an alternative antiseptic is povidone-iodine (based in alcohol) solution.

Once a catheter is *in situ* the appropriate dressing must be applied. Whenever possible this should be a semi-permeable, transparent, occlusive dressing. Dressing changes can be performed every seven days or sooner if required, for example, if moisture gathers underneath the dressing, providing a perfect environment for microbial growth[27]. If however, the insertion site is oozing or bleeding then a sterile gauze dressing would be more appropriate and this would need changing daily or when the gauze became damp, loose or soiled.

Best practice in the management and care of all infusion systems proposes the use of needle-free devices. Such devices must be used in accordance with manufacturers' recommendations otherwise the risk of catheter-related infections increases. As the hub is a focal point for infection or contamination it is recommended that that the hub be cleaned thoroughly with a chlorhexidine-based solution and allowed to dry before any manipulations take place[27]. In the past the use of in-line filters was thought to reduce the infusion-related phlebitis however, systematic review did not support their use in preventing CVAD associated infections[27].

Surveillance of infection rates has improved nationally but collation of local data through ward audit would be useful, so that trends and treatments can be examined and evaluated. Current national recommendations for central venous catheter management in relation to infection control are based upon the best available evidence. Many issues have been researched well and robust evidence consisting of systematic reviews and randomised controlled trials exist, but there is scope for further research.

Conclusion

This paper has attempted to provide an overview of catheter-related infections within the context of contemporary health care. The majority of infections seen in hospitalised neonates and children are nosocomial. Therefore it is the responsibility of HCWs to minimise the transfer of microbes using the means available within current practice. Many of the strategies and initiatives necessary are already common knowledge. What is required now is the willingness, motivation and determination of HCWs to integrate these strategies into their daily practice to ensure that optimal clean care is provided.

Within the current healthcare climate there are many challenges to overcome, but perhaps the biggest challenge of all is the fight between man and the microbe.

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