REVIEW ARTICLE

Intravascular-device infections

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Incidence of intravascular-device infections

Since the introduction of the plastic intravascular (i.v.) catheter (Meyers, 1945), parenteral drug administration, fluid replacement and nutrition have become important in patient care. However, complications associated with these devices, including septic thrombophlebitis and septicaemia, soon became apparent (Page *et al.*, 1952; Moncrief, 1958). The incidence of these complications varies according to the device used; e.g., bacteraemias have been reported in only 0.2–0.5% of patients with peripheral intravenous devices but in 3.8–12.0% of patients with central venous catheters (CVC) (Maki *et al.*, 1973). In total parenteral nutrition, septicaemia may also be a serious problem with an average of 7% of patients affected (Goldman and Maki, 1973). In a more recent and extensive multicentre study in Europe (Nystrom *et al.*, 1983), more than 10 000 surgical patients were investigated, 63% of whom were shown to have had an intravascular device inserted at some time during their hospital stay. Of these patients, 10.3% had a device-related thrombophlebitis, and 0.37% with a peripheral i.v. line and 4.48% with a CVC developed hospital-acquired bacteraemia. In comparison, only 0.05% of the patients without an i.v. device had bacteraemia in hospital.

The incidence of positive catheter culture and associated problems, including septicaemia, increases with the length of time the devices are left *in situ*, a finding confirmed in a recent cross-sectional survey in Newcastle (table I; T. S. J. Elliott, unpublished data). The recognition of this relationship has led to the recommendation that peripheral catheters should be replaced after 48 h, but this is not always practicable and can rarely be applied to CVC.

Microbiology of i.v.-device infections

The isolation of micro-organisms associated with

Table I. Relationship of duration of central venous cannulation to catheter-related complications*

Number of patients with	Duration (d) of cannulation		
	1–4	4–7	≥ 8
Catheters	9	29	46
Associated local infection	2	5	11
Associated septicaemia	0	3	3

* Data collected during a survey at Royal Victoria Infirmary, Newcastle-upon-Tyne between Dec. 1985 and Mar. 1987.

i.v.-device infections may be difficult. On occasions they may be cultured from swabs taken at the insertion site, particularly when there is evidence of localised infection. The results, however, may be misleading, particularly if skin commensals rather than recognisable pathogens are isolated. A more accurate method for determining which organisms are responsible for i.v. device-related sepsis is achieved by taking blood for culture both through the device and *via* another venepuncture site. Isolation of micro-organisms from blood taken through the catheter only is suggestive of a line-associated infection, whereas positive cultures from both blood samples may result from additional causes. The definitive method for identifying the micro-organisms associated with these infections is removal of the line and culture of its distal tip by any one of numerous techniques available for microbiological examination. In one commonly adopted approach, a short length (c. 3 cm) of catheter tip is rolled back and forth at least four times across the surface of a nutrient-agar plate (Maki *et al.*, 1977). However, if catheters are contaminated with skin flora on removal, any subsequently isolated micro-organisms may not be representative of the pathogen. Partially to overcome this problem, Maki *et al.* (1977) proposed a semi-quantitative culture method whereby infection could be distinguished from contamination.

They suggested that a colony count of > 15 cfu of the micro-organism from the sampled device indicated the presence of a pathogen and that a lower count represented contamination. This criterion is not universally accepted in many clinical microbiology laboratories where microbiologists prefer to assess a culture result with direct reference to the patient's condition. A further problem associated with the roll-plate technique is that it samples the external surface of the device only, although it has been demonstrated that microbial colonisation may occur on both external and internal surfaces (Cheesbrough *et al.*, 1985). Indeed, Cleri *et al.* (1980) suggested that after a catheter had been sampled by the roll-plate technique, the lumen should also be tested by flushing with broth which should then be inoculated on to appropriate nutrient-agar plates and incubated. This method of lumen sampling is also prone to difficulties. It does not allow quantitation of the microbial colonisation of the internal surface and if the i.v. line or broth is contaminated during removal, or in the subsequent manipulations, erroneous results may ensue. At present the roll-plate technique in conjunction with blood cultures seems the most appropriate and specific method for distinguishing contaminants from pathogens in catheter-related infections.

The micro-organisms most often implicated with i.v. device-related sepsis are usually those derived from the patient's skin although there is some evidence that hospital staff too may be an important source. The most common isolates from catheter tips are *Staphylococcus epidermidis*, *S. aureus*, streptococci and gram-negative bacilli, including species of *Klebsiella* and *Pseudomonas*. Not infrequently, species of *Candida* have also been cultured from i.v. devices. A corresponding range of organisms has been demonstrated in patients with catheter-associated septicaemia. More recently, *S. epidermidis* has emerged as the most important cause of i.v. device-related infections (Eykyn, 1984), being the commonest species reported from catheter-tip cultures in a review of eight prospective studies (Maki *et al.*, 1973). The apparent emergence of *S. epidermidis* as a line-associated pathogen may reflect partly the use of central lines for extended periods with increased infection rates, as well as the now universal acceptance of coagulase-negative staphylococci as pathogens. Furthermore, it has been suggested that if patients are already receiving antibiotics before development of a catheter infection, the causative organism is more likely to be an antibiotic multiresistant strain of *S. epidermidis* or a gram-negative bacillus rather than *S. aureus* (Eykyn, 1984). The use of broad-spectrum antibiot-

ics may similarly encourage infections with *Candida* spp.

Source of micro-organisms

Commensals on the patient's skin are probably the most important source of micro-organisms in i.v.-associated infections (fig. 1); some of these organisms gain access to the catheter, in particular the distal tip, at the time of insertion. Organisms may also migrate down the interface between the catheter surface and the skin (Elliott, 1987). Therefore adequate skin preparation before insertion is important in the prevention of these infections. It is generally accepted that most catheter-related sepsis, particularly those episodes associated with staphylococci, start as a local skin infection at the entry site of the catheter. With improved catheter care, however, other mechanisms of infection may now occur more commonly. Indeed, it has recently been suggested that catheter-hub colonisation represents the most important source of organisms. This was demonstrated in an outbreak of i.v. device-related infections by coagulase-negative staphylococci secondary to hub colonisation after manipulation by medical staff (Sitges-Serra *et al.*, 1984). Deitel *et al.* (1983) also reported i.v.-related sepsis with *S. epidermidis* after a defective catheter-hub attachment was associated with bacterial contamination. In a prospective study of 135 adult patients with subclavian catheters, Linares *et al.* (1985) further demonstrated a high proportion of infections resulting from colonised hubs and proposed that colonisation of the inner surface of the catheter hub was followed by intraluminal progression, tip infection and sepsis. A similar mechanism of sepsis was described with indwelling lines (Shinozaki *et al.*, 1983).

Colonisation of i.v. devices may also result, occasionally from contaminated infusions and haematogenous seeding. Outbreaks of infusion-related sepsis are rare and are predominantly derived from infusions contaminated during manufacture or administration in the hospital (Sack, 1970).

Although sideports have also been suggested as being responsible for an increased risk of hospital infection (Peters *et al.*, 1979; Oberhammer, 1980), it has not been clearly demonstrated that the infection rate associated with sideport cannulae is increased (MacFarlane *et al.*, 1980; Cowan, 1982). Contamination of sideports may result from incorrect care and management; e.g., if the sideport caps are left open or patients handle them, microbial contamination may ensue. Care of sideports,

Fig. 1. Schematic representation of a cross-section of the skin and underlying tissue at site of cannulation demonstrating potential source of micro-organisms causing line-associated infections.

therefore, is important in infection control. Sideports consisting of latex or similar membranes have been proposed as an alternative to the valved system. However, Jakobsen and Grabe (1983) have demonstrated that the use of these membranous sideports does not reduce the rate of contamination in comparison to the valved system. Furthermore, with the emergence of blood-borne diseases such as hepatitis B and AIDS, the need to use needles to give fluids *via* the membrane sideports, close to a venepuncture site which may be contaminated with blood products, is not ideal.

Irregular catheter surfaces have also been associated with increased thrombogenicity (Hecker, 1981; Hecker and Scandrett, 1985). A thrombus may form on catheters within hours of insertion (Hoshal *et al.*, 1971) and can entrap bacteria (Elliott *et al.*, 1984) forming a nidus of colonisation and eventual infection.

The process by which bacteria attach directly to the inner or outer surfaces of catheters involves

Table II. Some factors influencing microbial colonisation of intravascular devices

1. Patient
 - skin preparation
 - site and position of insertion
 - type of insertion; e.g., tunnelled
2. Medical personnel
 - hand washing before insertion
 - care and technique of insertion
 - care of insertion site
3. Intravascular device
 - design
 - cannula material
 - surface topography
 - leachable substances from catheter
 - catheter diameter
 - flow rate of infusion

Mechanisms of microbial colonisation

There are many factors that influence the microbial colonisation of intravascular catheters (table II), including the type of device, its design and catheter composition. Thus, Sheth *et al.* (1983) used an in-vitro model to demonstrate that adherence of coagulase-negative staphylococci to polyvinylchloride was greater than that to Teflon catheter. Again, the surface topography of the catheter also influences bacterial colonisation. The initial stage of bacterial attachment appears to be associated with surface irregularities (Locci *et al.*, 1981; Cheesbrough *et al.*, 1985) and the organisms attach predominantly to roughened areas (fig. 2).

three basic stages (table III). First, the micro-organisms must be attracted to the catheter surface, a process influenced by the physico-chemical surface properties of the organisms including free energy and electrical and hydrophobic charges. Other factors which may also affect this interaction are the relationship between the micro-organism's growth rate and its cell-wall composition. For example, the quantity of teichoic acid in the bacterial cell wall, partially determining the surface charge, may vary according to growth rate and availability of certain substrates. The initial attraction of micro-organisms to a catheter surface is

Table III. Stages of attachment of micro-organisms to intravascular catheters

Stage	Factors involved
1. Attraction of micro-organisms to proximity of catheter	Physicochemical surface properties: free energy; electrical charge; non-covalent forces; hydrophobicity
2. Firm attachment of micro-organisms to catheter	Physicochemical forces Production of glycocalyx Formation of thrombus
3. Multiplication of micro-organisms	Availability of nutrients Suitable conditions

complicated and probably involves a multiplicity of the above-mentioned factors. Further complications in understanding this process have arisen due to variability in methods used to identify these factors. This problem was emphasised recently by Dillon *et al.* (1986) who, in a comparison of 5 methods for assaying bacterial hydrophobicity, demonstrated that variable results were obtainable and concluded that reliance on one method alone was inadequate. After initial attraction to the catheter surface, some micro-organisms become firmly attached particularly at the distal end and often as rapidly as within 20 min (Elliott *et al.*, 1988). Some bacteria, including *S. aureus* and *S. epidermidis*, produce a slime layer also referred to as a glycocalyx (Costerton *et al.*, 1981). Bacteria may become embedded in this relatively thick layer of slime and so attachment is facilitated (fig. 2).

Bacterial capsules are generally firmly bound, compact structures with clearly defined boundaries whereas extracellular slime is loosely bound, water soluble and readily removed. Nevertheless, although recognised for over a decade, the chemical nature of bacterial slime is still not fully documented. There is some evidence that it is a complex glycoconjugate rather than a carbohydrate polymer. Tests have been devised to identify bacteria which produce slime, but the degree of disparity amongst

Fig. 2. Scanning electronmicrograph of slime-producing *S. epidermidis* attached to the roughened surface of an i.v. catheter. The microcolony is embedded in slime so that some cells are indistinct. Bar = 4 μ m.

them makes interpretation difficult. Christensen *et al.* (1982), for example, developed a test, based on the ability of coagulase-negative staphylococci to adhere to surfaces, that was thought to reflect slime production. These two characters may not be the same (L. McTaggart, personal communication).

After the firm adherence of bacteria to the surface of an i.v. device, cell division results in colony formation (Elliott *et al.*, 1984).

Prevention of catheter-associated infections

The skin flora has been implicated as a major source of micro-organisms in i.v.-related sepsis. Adequate hand cleansing is essential, therefore, before insertion of a catheter. The number of resident bacteria on the hands may be greatly reduced by washing with soap and water, but disinfection with ethyl alcohol 70% is more effective. Use of antimicrobial preparations, e.g. chlorhexidine or povidone-iodine, is indicated particularly in special units such as intensive care or during an outbreak. The insertion site should also be adequately cleaned to remove blood, mucus and other organic debris. A suitable skin preparation such as ethyl alcohol 70% or iodine 1% in alcohol 70% should then be applied and left for an appropriate period, before insertion of the catheter. Shaving of the skin around the catheter site may be necessary to aid the subsequent anchoring of the device, but removal of hair at the insertion site is of questionable value. Indeed, shaving may encourage microbial growth by providing further nutrients. Careful records should be kept to ensure that catheters, especially peripheral ones, are *in situ* for no longer than the recommended times. The catheter should be firmly anchored without occlusion of the cannulated vein, because that might precipitate thrombus formation. Occlusive non-permeable dressings should be avoided because they may increase local humidity and result in enhanced microbial growth, a phenomenon sometimes referred to as the "greenhouse effect".

After catheter insertion, application of topical antibiotics to the catheter site has been shown to reduce catheter infections (Moran *et al.*, 1965). The use of topical antibiotics may, however, disturb the normal commensal flora leading to the emergence of antibiotic-resistant bacteria or fungi (Zinner *et al.*, 1969). Application of topical antiseptics, active against both fungi and bacteria, to the insertion site and parts of the i.v. device, such as the hub, that are likely to become contaminated seems a more logical approach than the use of topical antibiotics. Indeed, some centres already recommend regular

spraying with an antiseptic such as povidone-iodine over the hub to reduce contamination. Evaluation of that approach is awaited.

It is well recognised that bacteria attached to cannula surfaces may survive exposure to apparently lethal concentrations of antibiotics. For example, Sheth *et al.* (1985) demonstrated that slime-producing coagulase-negative staphylococci, when attached to polyvinyl chloride, survived exposure to nafcillin to which they were sensitive as judged by conventional testing. More recently, it has been demonstrated that slime-producing strains of *S. epidermidis* can attach to, and survive on, catheter surfaces in the presence of certain β -lactam agents, such as flucloxacillin, at concentrations above their minimum inhibitory concentrations (Elliott *et al.*, 1988). However, when inhibitory concentrations of ciprofloxacin or vancomycin were used, bacterial colonisation of catheters was reduced (Elliott, 1988). Clinical application of the use of subinhibitory concentrations of antibiotics to prevent colonisation without selecting resistant strains is conceivable, but further evaluation is required. Current evidence suggests that once *in vivo* colonisation of a catheter has occurred, antibiotics (especially those acting on the cell wall) given through the line are usually ineffective in eradicating this potential focus of infection.

Clinical approach to catheter infections

Care of the catheter after insertion is also important to prevent contamination and eventual microbial colonisation. The insertion site should be regularly inspected for any evidence of infection and peripheral catheters should be replaced every 48 h. The development of a fever in a patient with a catheter or phlebitis at the infusion site should suggest that the catheter is the source of infection. Phlebitis is not always present, however, and infusion-related septicaemia may be indistinguishable from sepsis of other causes. Continued symptoms and signs of systemic infection, despite appropriate antimicrobial therapy, are typical. Occasionally, eradication of line-associated sepsis may be achieved with antibiotics. When, however, colonisation of an i.v. catheter is strongly suspected it should be removed and examined for the presence of micro-organisms. Removal of the catheter usually resolves infection in most patients. Antibiotics are also occasionally given on removal of the line, particularly if another catheter is to be inserted or the patient has exhibited evidence of a septicaemia. Sometimes it is necessary, on clinical grounds, to keep an i.v. device *in situ* despite the

fact that it has been colonised and has been associated with infection. In such a situation, appropriate samples for microbiological investigation must be taken and treatment with antimicrobials started so that complications, e.g., metastatic abscess formation or colonisation of other sites such as the heart valves, are avoided. The most appropriate antibiotic to give will depend on previous culture and antibiotic-sensitivity results, particularly of micro-organisms from cultures of blood taken through the line or from swabs of an infected i.v. site. The choice of antibiotics should also take into account the patient's current therapy and significant microbial isolates from other sites. Antibiotic susceptibility of the organisms, predominantly the staphylococci associated with i.v. lines, is difficult to assess. Flucloxacillin is acceptable for *S. aureus* except in centres where multiresistant strains are present. In comparison, *S. epidermidis* sensitivity is less predictable because many strains are multiresistant with vancomycin as the only available "treatment".

Future developments of prevention of i.v. device-related sepsis

It is apparent that prevention of line-associated infections is preferable to cure. Perhaps regular specialised training of medical personnel in the correct techniques of catheter insertion should be widely adopted. Properties of the materials and methods used in cannula production also need to be developed. Ideally the i.v. lines should be inert, and have smooth surfaces from which no substances leach out, so that bacterial attachment and thrombus formation is prevented. Incorporation of antibacterial agents in catheters is another approach but problems of stability and leaching, together with the possibility of the emergence of resistant organisms, remain. Currently, however, it is apparent that awareness of line-associated infections, with adoption of appropriate preventative measures by collaboration between clinicians and microbiologists, is one of the most important control factors.

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