Diagnosis of central venous catheter related sepsis—a critical look inside

B M Dobbins, P Kite, M H Wilcox

The use of central venous catheters for the administration of pharmaceutical agents, including chemotherapy regimens, inotropic support in the intensive care setting, intravenous nutrition, cardiac monitoring, and as a means of maintaining long term venous access, has increased dramatically in the past three decades. Complications associated with central venous catheterisation include those associated with insertion—for example, pneumothorax, haemorrhage, nerve injury, catheter tip misplacement, and cardiac arrhythmias—and those associated primarily with longer term use, including thrombosis and infection. Catheter related infections represent by far the greatest risk associated with the use of central venous catheters, and the rate of catheter related sepsis is variably reported to range from 4% to 14%.[1–4] The magnitude of this variance reflects true differences in the incidence of catheter related sepsis in some patient groups—for example, the rate of catheter related sepsis in burns patients managed in intensive care is approximately 15-fold higher than in those with respiratory disease.[5] Infections associated with central venous catheters therefore represent approximately 30 000 and 400 000 cases in the United Kingdom and the USA, respectively, each year.[6] However, differences in the reported incidence of catheter related sepsis also result from a lack of standardisation in diagnostic approach.

Catheter related sepsis is associated with significant morbidity and mortality, and with case fatality as high as 10–20%.[7] Major complications of sepsis were reported in 32% of cases in one series.[8] There has been a two- to threefold increase in the cases of primary nosocomial bloodstream infections in the last decade,[9] the large proportion of which have been attributed to catheter infections. The incidence of hospital acquired infection in a recent surveillance study was sevenfold higher in patients with an invasive device.[10] Catheter related sepsis represents a significant burden to the health service, and the excess hospital cost associated with these bloodstream infections has been estimated at $40 000.[11] Another report calculated the cost of a single episode of catheter related sepsis in patients on an intensive care unit (ICU) as up to $28 000.[12] Episodes of catheter related sepsis cause a major proportion of the septicaemias due to coagulase negative staphylococci, *Staphylococcus aureus*, and *Candida* spp. This review aims to discuss contentious issues relating to the aetiology and diagnosis of catheter related sepsis, and to challenge some beliefs using recently available data.

Department of Microbiology, University of Leeds, Leeds LS2 9JT, UK
P Kite
M H Wilcox

Department of Surgery, University of Leeds
B M Dobbins

Correspondence to:
Dr Wilcox.
email:
markwi@pathology.leeds.ac.uk

Accepted for publication
2 November 1998

Definitions

Perhaps one of the greatest difficulties in reviewing the subject of central venous catheter infection is the large variation in what is considered to be an "infected catheter." This problem appears to have arisen as a result of the many methods which have been described to culture catheters. In addition to the multitude of catheter culture techniques much debate still exists as to precisely what is a significant quantity of bacterial growth. Central venous catheters are inserted through and reside in close proximity to skin containing approximately 10^5–10^6 bacteria/cm^2. Furthermore, approximately 10^8 skin scales/person are shed daily, about 10% of which contain bacteria. Hence, separating infected, colonised, and contaminated central venous catheters can be extremely problematic. Furthermore there is no gold standard method whereby all techniques for the diagnosis of central venous catheter infection can be compared, and thus the vast majority of sensitivities and specificities quoted should be critically assessed and cannot be taken at face value. Despite these shortcomings, there is a generally accepted definition of catheter related sepsis (or catheter related bacteraemia) which requires the following three criteria to be present:

(1) A significantly positive catheter culture (although the definition of "significant" is contentious).
(2) A positive peripheral blood culture taken before catheter removal.
(3) The same microorganism isolated in both (1) and (2).

By insisting on the presence of an associated peripheral bacteraemia this allows for more accurate comparisons of methodology and diagnosis of catheter related sepsis. However, the significance of a colonised catheter in the absence of a systemically proven infection can be strongly debated. While it is accepted that a positive catheter culture in the absence of peripheral bacteraemia may occasionally represent either poor peripheral blood sampling or even a transient fall in peripheral bacterial load at the time of sampling, it is the only method by which one can truly compare all of the methods for the detection of catheter related sepsis. Unfortunately, blood culture contamination by skin microorganisms is common, and recent studies have highlighted the low positive predictive value of blood cultures positive for coagulase negative staphylococci.[13 14] For example, of 89 blood cultures positive for skin flora, 91% involved coagulase negative staphylococci, and the incidence of significant and indeterminate coagulase negative staphylococcal bacteraemia and of contamination was

found to be 25%, 12%, and 73%, respectively.[14] While part (3) of the above definition of catheter related sepsis states that the "same" microorganism is isolated from the central venous catheter and from peripheral blood cultures, it is often assumed that bacteria sharing the same antibiogram or biotype are indeed the same; we have found that of 21 coagulase negative staphylococcal pairs isolated from peripheral blood cultures and central venous catheters, five (24%) were in fact distinguishable by DNA fingerprinting despite most sharing the same biotype.[15]

Clinical definitions of catheter infections and catheter related sepsis are not infrequently used. These definitions rely on the absence of any other demonstrable cause for a patient's sepsis. However, patients requiring central venous access are often unwell, immunosuppressed, or have often undergone surgery and are therefore likely to have alternative potential sources of infection. Of those suspected and subsequently proven to have catheter related sepsis, 50% had a documented potential alternative focus of sepsis (that is, other than the catheter itself); 63% of the remainder who did not have proven catheter related sepsis also had a documented potential alternative focus of infection.[16] Furthermore, in a study of 109 cases of clinically suspected catheter related sepsis only 40 were confirmed after microbiological culture. Using both pyrexia and leucocytosis as clinical indicators, no significant difference was observed between groups proven to have or not to have catheter related sepsis.[16] Evidence of inflammation at the catheter skin entry site does not necessarily represent catheter infection but may merely be caused by local irritation from the central venous catheter. Nevertheless localised infection does occur at the skin entry site and in its most florid form is seen as tunnel tract sepsis which may give rise to abscess formation. Such infections should perhaps be considered as wound infections in the presence of a foreign body.

Diagnostic methods for catheter related sepsis

PERIPHERAL BLOOD CULTURES

As already indicated the confirmation of a peripheral bacteraemia is paramount in the diagnosis of catheter related sepsis. The peripheral blood sample should be obtained while the central venous catheter is in situ and not after removal. The peripheral blood cultures should ideally be taken while the patient is pyrexial, and blood samples should be obtained from separate peripheral sites, although for practical purposes often only one peripheral set of blood cultures is collected. Endoluminal colonisation of the central venous catheter results in the infusate flowing over heavily colonised endoluminal biofilm containing both sessile and planktonic forms of bacteria. The planktonic bacteria enter the infusate and thereafter the systemic circulation. The infusate should not therefore be stopped before peripheral blood sampling. In cases of catheter related sepsis secondary to extraluminal colonisation alone (see below) the sampling of peripheral blood should not theoretically be governed by flow through the catheter. Qualitative blood cultures are readily available in all hospitals and have the advantage of being both relatively inexpensive and easy to process. However, quantitative blood cultures are considered to be both more accurate and less likely to produce false positive results owing to contamination during sampling. Quantitative analysis of blood samples taken from adults and children clearly indicates that the magnitude of bacteraemia is greater in infants. Most episodes of clinically significant bacteraemia in adults are characterised by low numbers, and for example, Henry *et al* found < 1 colony forming unit (cfu)/ml in 27%, 55%, and 62% of cases of *S aureus*, *P aeruginosa*, and *E coli* bacteraemia, respectively.[17] Of 43 cases of catheter related sepsis from our studies, peripheral bacteraemic counts were < 1 cfu/ml in 30% of cases (Kite P, Dobbins B, Wilcox M, unpublished data). It is recommended therefore that at least 10 ml of peripheral blood are sampled for each blood culture to reduce the likelihood of false negative results.

The pour plate technique of quantitative blood culture involves mixing blood and molten agar and then pouring them into a Petri dish.[18] The spread plate technique involves spreading blood across the surface of an agar plate.[18] Both methods have the disadvantage of only allowing < 1 ml of blood/plate, and numerous plates (up to 10/sample) need to be plated for accurate assessment. A lysis centrifugation technique for the analysis of blood cultures has been developed in the form of isolator microbial tubes (Unipath). Developed from an original technique described by Dorn *et al*,[19] this technique is designed to maximise the detection of low magnitude bacteraemia or fungaemia and to remove inhibitory factors such as antibiotics that may be present in blood. The technique has proven benefits of isolation of a wide range microorganisms, and has been shown to be superior to broth culture methods by increasing recovery of microorganisms from 67% to 80%.[20 21] It has also been shown to inhibit phagocytosis and enhance speed of culture, and it is less cumbersome than other quantitative techniques. However, variable rates of contamination from 1.4% to 10.9% have been reported,[21] and these are comparable with other surface spread techniques. The technique is, however, expensive and time consuming in comparison with qualitative blood cultures.

CENTRAL VENOUS CATHETER CULTURE

Central venous catheter culture methods involve culturing catheter segments, usually the distal end but proximal (primarily subcutaneous) sections in some cases, and accurate comparison of differing techniques can be extremely difficult. Indeed, the length of catheter segments which are sampled is poorly standardised, and in the original description of the Maki roll technique sections between 5 and 7 cm in length were sampled.[22] Techniques can also be divided according to whether the external surface of the central venous catheter, the

endoluminal surface, or both environments are sampled. While a positive catheter culture in the presence of peripheral bacteraemia is all that is required to make a diagnosis of catheter related sepsis, a negative catheter culture made without assessing the whole of the catheter does not exclude the diagnosis. For practical purposes, in vitro sampling of the whole of the catheter (extraluminal and endoluminal surfaces, from hub to tip) is not a cost–effective or time–effective method of assessing central venous catheters, and thus a compromise method of analysis has often been used. However, in the study setting and in the interest of good science, assessment of the whole of the catheter should be undertaken, to act as a gold standard with which other central venous catheter culture methods can be compared. Unfortunately few studies have looked at all aspects of central venous catheter colonisation.

Specific central venous catheter tip culture techniques

QUALITATIVE CULTURE

A qualitative culture technique described by Druskin and Siegel in 1963 involved the immersion of the catheter tip in broth, with any growth of the catheter being significant.[23] The obvious disadvantage of this method is the relatively high level of false positive results; these led to development of both quantitative and semi-quantitative methods of catheter tip assessment.

QUANTITATIVE CULTURE

Seligman first proposed the use of quantitative culture of the catheter tip.[24] The techniques of microorganism retrieval and catheter culture have been modified over the ensuing years in order to improve the sensitivity and specificity of this approach. Flushing the catheter tip, vigorous agitation, sonication, vortexing, and a combination of sonication and vortexing have all been described as methods of releasing the microorganisms entrapped in the catheter biofilm.[25] The threshold levels for these various techniques vary from between 100 and 1000 cfu/ml,[25] and as a result sensitivities and specificities are accordingly affected. Both the internal and external surfaces of the catheter tips are cultured with such qualitative and quantitative methods, and thus the relative contributions of each to catheter related sepsis cannot be deduced from these results.

In 1977 Maki *et al* described a method of catheter culture which was to become the standard method for central venous catheter analysis over the next 20 years.[22] The original study was performed primarily (87%) on peripherally inserted cannulas, 85% of which were short catheters (mean length 5.7 cm), but the technique offered a simple, inexpensive, and seemingly accurate method of catheter culture. In this technique the external surface of the catheter tip is sampled and as few as 15 cfu are considered as a significant bacterial yield, although Maki himself acknowledged a higher value of 1000 cfu as more accurately predicting cases of catheter related sepsis.[21 22] Furthermore, only four of 13 catheters which had Maki roll counts of > 1000 cfu were actually from patients diagnosed as having catheter related sepsis, so indicating the low specificity of this method.[22] The Maki roll technique and the above tip culture techniques are prone to contamination of the external surface of the catheter tip segment upon removal through colonised skin entry sites, which—combined with the low cut off values of 15 cfu often used—produces difficulty in interpreting catheter tip culture results. Terms such as catheter contamination, catheter colonisation, and catheter infection are often applied to interpret various degrees of catheter microbial bioload not associated with a peripheral bacteraemia, and are invariably confused and misinterpreted as true cases of catheter related sepsis. A study looking at both clinically suspected and routinely removed non-suspected triple lumen catheters (100 catheters studied) showed no significant difference in the proportion of Maki positive results or the degree to which the external portions of the catheter tips were colonised, despite 25 cases of proven catheter related sepsis in the suspected group and none in the routinely removed central venous catheters.[26] Furthermore, this study showed a strong correlation between the number of microorganisms yielded by the Maki technique and the magnitude of microbial growth after sampling skin around the catheter entry site. Elsewhere, the positive predictive value of the roll plate method has been found to be in the range of 10–75%.[27 28]

The accuracy and clinical significance of the above techniques are more helpful when the microorganism isolated is not a typical component of the skin microflora—for example, yeasts and Gram negative bacilli—in which cases the results are unlikely to represent central venous catheter contamination. The converse of this is illustrated in table 1, which summarises the composite results of colonised and infected central venous catheters, as defined by two endoluminal methods and the Maki roll technique.[29] It can be seen that coagulase negative staphylococci were apparently significantly more often associated with colonisation as opposed to infection, whereas the reverse was true for Gram negative bacilli with a similar trend for *S aureus*. These results probably arise from the excess proportion of central venous catheters identified as being colonised by the Maki roll technique (92%)

Table 1 Microorganisms causing catheter related sepsis and catheter colonisation (reproduced from reference 29)

	Number (%) of episodes	
Microorganism¶	*Colonisation (n=76)*	*Catheter related sepsis (n=22)*
Coagulase negative staphylococci	63 (83)***	9 (41)***
Staphylococcus aureus	5 (7)*	4 (18)*
Enterococci	5 (7)	3 (14)
Gram negative bacilli	1 (1)**	4 (18)**
Candida spp	1 (1)	2 (9)
Other	1 (1)	0

¶Predominant microorganism in the case of mixed growth. *0.1>p>0.05; **p<0.01; ***p<0.001, statistical comparison of the percentage of colonisation *v* catheter related sepsis episodes for each microorganism.

compared with those detected by the endoluminal methods (43%).[29] When the Maki roll method has been employed, it has been estimated that up to 75–85% of central venous catheters are removed unnecessarily on clinical suspicion of catheter related sepsis,[30 31] and the risks of complications following central venous catheter reinsertion are not insignificant.[30] Nevertheless, an advantage of the technique is that in cases of true catheter related sepsis the source of infection is removed immediately, even though the diagnosis is only made 24–48 hours after removal.

CATHETER TIP FLUSH TECHNIQUES

The catheter tip flush technique was originally described by Cleri *et al.*[32] One modification, aimed at removing microorganisms from the outer surface of the central venous catheter tip, has been shown to be as sensitive as the methods described above but in addition is more specific for the diagnosis of catheter related sepsis.[29] The enhanced specificity results either from the reduced false positive culture rate associated with contamination of the external surface of the catheter, or from the assumption that endoluminal as opposed to extraluminal catheter colonisation is more significant in the development of catheter related sepsis.

Attempts to overcome some of the inaccuracies of catheter tip culture have included the sampling of numerous segments of both the catheter tip and the tunnelled segments of the catheter proximal to the tip.[32 33] However, such techniques are complicated, difficult to interpret and unless the extraluminal and endoluminal surfaces are differentially cultured, remain prone to contamination, as discussed earlier.

Other catheter sampling techniques

ENDOLUMINAL BRUSH

Endoluminal catheter sampling was first described by Grabe and Jakobsen in 1983,[34] who used a steel stiletto inserted into the lumen of the catheter; the technique was later improved by the use of an endoluminal brush by Marcus and Buday in 1989.[35] It involves introducing a sterile endoluminal brush (FAS Medical) through a Luer lock attached to the catheter hub and advancing it through the catheter. Upon removal the brush is clipped off and, together with any adherent luminal biofilm, is vortexed in 1 ml of phosphate buffered saline and then quantitatively cultured (colony counts of > 100 cfu being regarded as significant). In 230 central venous catheters used predominantly for total parenteral nutrition (median dwell 9.5 days) we found that of 22 (10%) causing sepsis, 17 yielded significant growth from both surfaces, four from the inner surface alone, and one from the outer surface alone.[29] In this cohort, the sensitivity and specificity of the endoluminal brush technique for the diagnosis of catheter related sepsis were 95% and 84%, respectively. Recent re-evaluation of the technique has shown maintained sensitivity but improved specificity when the brush is passed to within approximately 5 cm of the catheter tip (that is, until resistance to progress of the brush is detected owing to catheter narrowing), and not through the catheter tip as first described.[36] Quantitative peripheral blood cultures before and after brushing in 43 cases of proven catheter related sepsis revealed no significant increase in the mean bacterial count at either three minutes or one hour after brushing.[37] Unlike other methods of catheter evaluation, this approach does not require the needless sacrifice of catheters to evaluate suspected cases of catheter related sepsis. However, diagnostic quandaries exist when investigating multilumen central venous catheters. In a study of 100 triple lumen catheters in which catheter related sepsis was identified in 25 cases, 40%, 40%, and 20% of the catheters had one, two, and three lumens significantly colonised.[26] Hence a decision has to made about whether to sample the catheter lumen which has been used most often (particularly for total parenteral nutrition) or to assess multiple lumens.

CATHETER HUB CULTURE

The catheter hub has often been treated as a separate part of the central venous catheter in many studies of catheter related sepsis. Results of catheter hub studies have therefore been used as a means of assessing the route taken by microorganisms in order to reach the catheter tip, rather than as a possible source of catheter sepsis of itself. Sitges-Serra and colleagues showed that hub culture was positive (> 1000 cfu) in 14 of 20 documented cases of catheter related sepsis (70%).[38] In our own studies of 60 cases of catheter related sepsis, culture of hub swabs yielded > 100 cfu in 70% of cases (Kite P, Dobbins B, Wilcox M, unpublished data). The hub is, however, often cleaned with an antiseptic and as a result culture may be negative but the lumen just distal may be significantly colonised. The major advantages of both endoluminal and hub culture techniques are that they can both be performed on central venous catheters in situ, thereby reducing the number of catheters that are needlessly sacrificed to enable other culture techniques to be performed. An iodine chamber/hub device has been shown to reduce catheter related sepsis rates fourfold.[39 40] However, aseptic handling is still required when attaching the device to the catheter hub.

Indirect methods of central venous catheter culture

QUANTITATIVE BLOOD CULTURES

Paired quantitative culture techniques rely on the principle that blood aspirated over a colonised catheter lumen will contain proportionately more organisms than peripheral blood cultures as a result of haemodilutional effects and, more importantly, because of the reticuloendothelial system present in the lung and its ability to remove bacteria from the circulating blood. Various methods of quantification of the blood cultures (described above) have been used in the assessment of central venous catheters. The relative proportions of catheter to peripheral blood bacteraemia range from 1:4 and 1:30.[41 42] Such techniques are accurate

for the diagnosis of catheter related sepsis and again do not rely on catheter removal. However, in our experience blood cannot be aspirated in between 12% and 25% of cases, and published data indicate that this may be the case in up to 50%[33]; thus the technique is not as accurate as it appears if all central venous catheters are assessed. Furthermore, right atrial blood can be assumed to have higher bacterial counts than peripheral blood in cases where there is a distant source of sepsis as the blood has yet to be filtered by the pulmonary vascular system.[43]

ENTRY SITE CULTURE

Skin entry site cultures have been used to both predict and diagnose catheter infections.[44] Interpretation of positive results can be difficult as skin microbial colonisation may be transitory and can vary markedly between patients. Not surprisingly an association with positive skin culture and catheter tip culture has often been reported,[45 46] but this may simply reflect the contamination of the catheter tip upon removal. Clinical signs of suppuration, tract erythema, and even abscess formation represent catheter wound infections and do not necessarily correlate with catheter related sepsis; these should be viewed as separate types of infective catheter complication.

Rapid diagnostic techniques

DIRECT CATHETER STAINING TECHNIQUES

Direct staining of the catheter tip or impression smears of catheter segments upon removal have been described, using both Gram and acridine orange stains.[47–49] The obvious advantage of this approach is early diagnosis and therefore earlier treatment. However, as catheter removal is required, unnecessary sacrifice is inevitable, and furthermore antibiotic susceptibilities still take a minimum of 24 to 48 hours from the time of removal. The technique is just as prone to contamination as other tip culture methods and the procedures are tedious and time consuming, mainly owing to the requirement for focusing on a field of cellular material on a curved and often non-transparent material.

ACRIDINE ORANGE STAINING OF CATHETER BLOOD

Kite and colleagues described a rapid acridine orange/Gram stain technique for the examination of cytospun catheter blood samples.[49 50] The technique requires as little as 50 ml of blood and results can be obtained in about 30 minutes, thus allowing early diagnosis and treatment of serious infections such as Gram negative bacterial and fungal sepsis. The sensitivity and specificity of this techniques were 85% and 94%, respectively, when a group of 95 neonates and infants was studied.[50] The method is also applicable to adults, with a sensitivity and specificity of 96% and 94%, respectively, in 60 episodes of catheter related sepsis.[49 50] However, as stated previously the method is limited by the frequent unavailability of through line catheter samples owing to line blockage, and also the requirement for specialist equipment.

Other catheter related sepsis detection approaches

ELECTRON MICROSCOPY

Scanning electron microscopy has been used in the research setting to evaluate catheter colonisation. Raad *et al* examined the extraluminal and endoluminal surfaces of central venous catheters by semiquantitative electron microscopy.[51] They visualised microbial colonisation of all central venous catheters examined, including 39 associated with catheter infection and 26 culture negative controls. The extent of endoluminal surface coverage by biofilm (in catheters obtained premortem) was greater than for extraluminal surfaces. While the extent of biofilm coverage on extraluminal surfaces essentially remained unchanged with increasing duration of central venous catheter placement, the percentage of colonised endoluminal surface increased with time. Central venous catheters (n = 10) recovered postmortem generally had a greater percentage of their extraluminal surfaces covered by microbial biofilm than catheters obtained premortem; the likely explanation for this is that biofilm may be lost owing to shearing upon removal of the central venous catheter.

Our own electron microscopic studies of catheters causing sepsis have shown copious endoluminal but not extraluminal biofilms comprising microbes, extracellular material, and fibrin (fig 1). Culture results confirmed the relative contributions of endoluminal and extraluminal catheter colonisation to catheter related sepsis. Furthermore, these findings were consistent regardless of the species of bacteria or fungi isolated. In some cases positive extraluminal cultures were obtained, but we were unable to demonstrate microorganisms on the external surface of the catheter by electron microscopy, possibly reflecting the relative insensitivity of the latter approach or removal of biofilm during catheter withdrawal.

Recent evidence of the aetiology of catheter related sepsis

While the aetiology of catheter related sepsis, and in particular the potential routes of infection, has been extensively reviewed,[33 52 53] insight into the main contentious issue, namely the relative importance of the extraluminal and endoluminal routes of infection, has recently become available with the exciting development of antimicrobially impregnated/coated catheters.[54] At first glance, the results of such studies have been conflicting and often confusing. A large study of chlorhexidine and silver sulphadiazine coated catheters suggested a reduction in both colonisation and catheter related sepsis rates,[55] but later reports have failed to substantiate the initial findings.[56–58] These catheters are coated externally alone, which may explain the conflicting results. Interestingly, the use of impregnated cuffs on catheters, on the premise that extraluminal catheter colonisation is the main source of catheter infection, also gave inconsistent

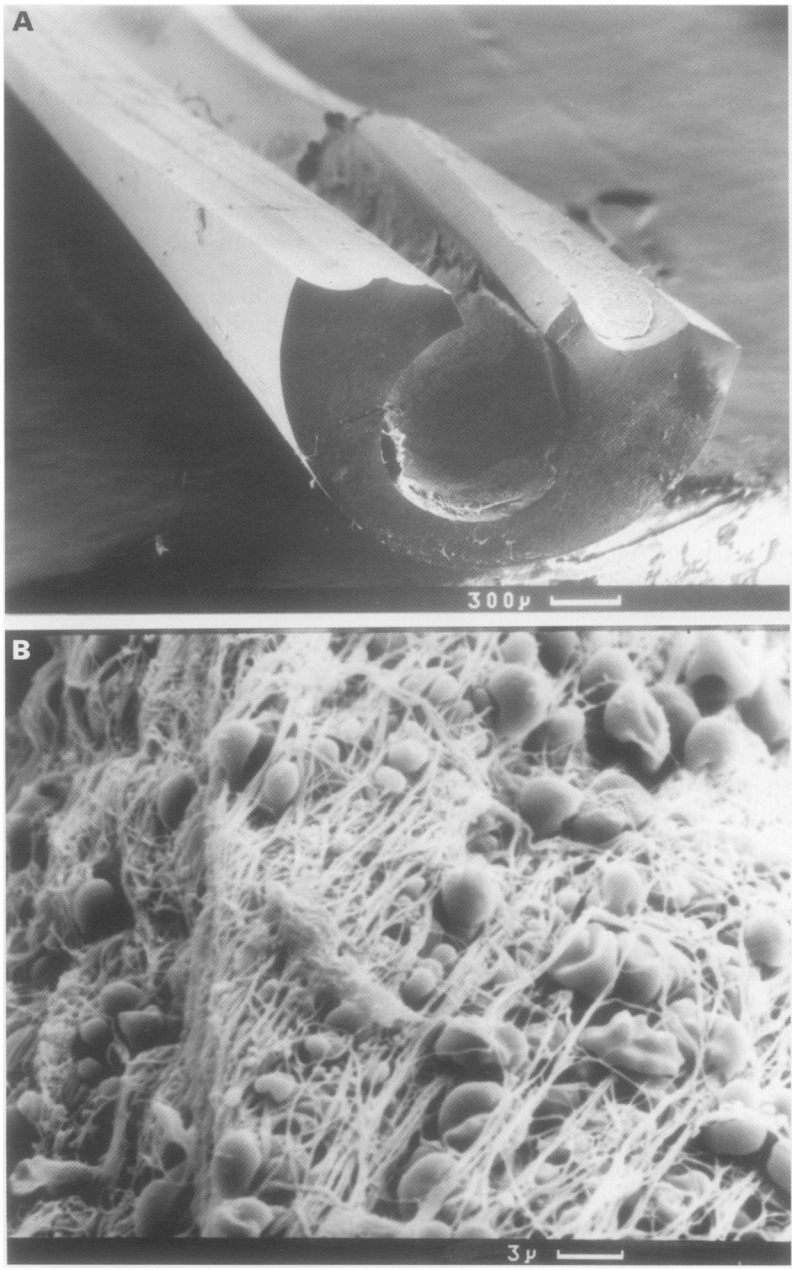

Figure 1 (A) Scanning electron micrograph of a split triple lumen central venous catheter showing yeast infected endoluminal biofilm in two lumens of a confirmed case of yeast catheter related sepsis with negative extraluminal surface. (B) High magnification scanning electron micrograph of the same central venous catheter showing yeast cells enmeshed in a blood fibrin matrix.

results.[59-61] Recent published data on the protective efficacy of rifampin and minocycline coated catheters have shown even more encouraging results.[62 63] However, although these catheters are coated on both outer and inner surfaces, the manufacturers have failed to coat the extracorporeal portion of the catheter from the hub to the catheter manifold (as in the silver/chlorhexidine catheter).[64] This area of the catheter represents over half the luminal surface area, and therefore there is still potential for endoluminal biofilm formation with consequent showering of bacteria into the circulation.

One of the most dramatic reductions in catheter infections and more specifically catheter related sepsis has been the introduction of dedicated teams to insert and manage central venous catheters (for example, hub care, skin entry site dressing, and giving set changes).[65] Such teams are common in the USA but not in the United Kingdom. It is assumed that this approach reduces the likelihood of central venous catheter contamination during insertion and subsequent manipulations. It is interesting to note that despite taking maximal precautions during central venous catheter insertion (experienced anaesthetists using strict aseptic technique in an operating theatre), Elliot and colleagues could demonstrate the presence of bacteria on five of 30 catheter tips (16%) within 90 minutes of placement into patients undergoing cardiac surgery. When central venous catheters were inserted through a protective Swan sheath the bacterial isolation rate was reduced to 1/30 (3%).[66 67] The fate of bacteria introduced onto central venous catheter tips at the time of insertion remains unknown, but it is disturbing that relatively high incidences of catheter seeding can occur in the hands of experienced operators, and in the face of cefuroxime (given as surgical prophylaxis).

Conclusions

In summary, the diverse methods which have emerged for the diagnosis of catheter related sepsis have not surprisingly yielded inconsistent findings. Critical appraisal of diagnostic methods tends to show a greater agreement for techniques that assess the catheter lumen as opposed to those which sample extraluminal surfaces. Clinical microbiologists and clinicians should together review the value of their current practice for the diagnosis of catheter related sepsis. Without such a critical approach wasteful and misleading rituals may persist. For example, it was found that Maki roll cultures of central venous catheters removed from surgical ICU patients had no clinical impact in 96% of episodes, and indeed a new line was inserted in the great majority of cases (86%).[68] It is clear that in the majority of cases where catheters are currently suspected of causing sepsis this is not confirmed, and hence the catheters are needlessly removed. Furthermore, a recent United Kingdom survey highlighted the frequent practice of empirical central venous catheter replacement in the ICU setting, despite the absence of supportive, prospective, randomised data.[69] Unnecessary catheter removal and replacement is costly and not without risk to the patient. Diagnostic methods for catheter related sepsis which are not reliant on line sacrifice are available, and can be exploited to overcome the problems created by this practice.

1 Michel L, McMichen JC, Bachy JL. Microbial colonisation of indwelling central venous catheters: statistical evaluation of potential contaminating factors. *Am J Surg* 1979;**137**:745–8.
2 Powell C, Kudsk KA, Kulich PA, *et al.* Effect of frequent guidewire change on triple lumen catheter sepsis. *J Parenter Enter Nutr* 1988;**12**:464–5.
3 Prager RL, Silva J. Colonisation of central venous catheters. *South Med J* 1984;77:458–61.
4 Gil RT, Kruse JA, Thill-Baharozian MC, Carlson RW. Triple versus single-lumen central venous catheters. A prospective study in a critically ill population. *Arch Intern Med* 1989;**149**:1139–43.
5 Jarvis WR, Edwards JR, Culver DH, *et al.* Nosocomial infection rates in adult and pediatric intensive care units in the United States. *Am J Med* 1991;**91**(suppl 3B):185–91S.

6 Raad II, Darouiche RO. Catheter related septicaemia: risk reduction. *Infect Med* 1996;**13**:807–12; 815–16; 823.
7 Maki DG, Cobb L, Garman JK, *et al.* An attachable silver-impregnated cuff for the prevention of infection with central venous catheters: a prospective randomised multicentre trial. *Am J Med* 1988;**85**:307–14.
8 Arnow PM, Quimosing EM, Beach M. Consequences of intravascular catheter sepsis. *Clin Infect Dis* 1993;**16**:778–84.
9 Banerjee SN, Emori TG, Culver DH, *et al.* Secular trends in nosocomial primary bloodstream infections in the United States, 1980–1989. *Am J Med* 1991;**91**:87–9S.
10 Glynn A, Ward V, Wilson J, *et al. Hospital-acquired infection. Surveillance, policies and practice.* A report of the control of hospital-acquired infection in nineteen hospitals in England and Wales. London: Public Health Laboratory Service, 1997.
11 Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infections in critically ill patients. Excess length of stay, extra cost, and attributable mortality. *JAMA* 1994;**271**: 1598–601.
12 Heiselman D. Nosocomial bloodstream infections in the critically ill. *JAMA* 1994;**272**:1819–20.
13 Herwaldt LA, Geiss M, Kao C, *et al.* The positive predictive value of isolating coagulase-negative staphylococci from blood cultures. *Clin Infect Dis* 1996;**22**:14–20.
14 Souvenir D, Anderson DE, Palpant S, *et al.* Blood cultures positive for coagulase-negative staphylococci: antisepsis, pseudobacteraemia and therapy of patients. *J Clin Microbiol* 1998;**36**:1923–6.
15 Kindon AJL, Dobbins BM, Fitzgerald P, *et al.* DNA fingerprints of coagulase-negative staphylococci isolated from catheters using a novel endoluminal brush [abstract]. Eighth International Symposium on Staphylococci and Staphylococcal infections, Aix Les Bains, France, 1996: 17.
16 Dobbins BM, Tighe MJ, Kite P, *et al.* Should in-situ endoluminal brushing of central venous catheters become part of the standard septic screen? [abstract]*Clin Nutr* 1997;**16** (suppl 2):73.
17 Henry NK, McLimens CA, Wright AJ, *et al.* Microbiological and clinical evaluation of the isolator lysis–centrifugation blood culture tube. *J Clin Microbiol* 1983;**17**: 864–9.
18 Tilton RC. The laboratory approach to the detection of bacteraemia. *Annu Rev Microbiol* 1982;**36**:467–93.
19 Dorn GL, Burson GG, Haynes JR. Blood culture technique based on centrifugation; clinical evaluation. *J Clin Microbiol* 1976;**3**:258–63.
20 Dorn GL, Burson GG, Haynes JR. Improved blood culture technique based on centrifugation; clinical evaluation. *J Clin Microbiol* 1979;**9**:391–6.
21 Yagupsky P, Nolte FS. Quantitative aspects of septicaemia. *Clin Microbiol Rev* 1990;**3**:269–79.
22 Maki DG, Weis CE, Sarafin HW. A semi-quantitative culture method for identifying intravenous-catheter-related infection. *N Engl J Med* 1977;**296**:1305–9.
23 Druskin MS, Siegel PD. Bacterial contamination of indwelling intravenous polyethylene catheters. *JAMA* 1963;**185**: 966–8.
24 Seligman SJ. Quantitative intravenous catheter cultures identify focus of bacteraemia [abstract]. Abstracts of the Annual Meeting of the American Society of Microbiology, Chicago, 1974:M18.
25 Kristinsson KG, Burnett IA, Spencer RC. Evaluation of three methods for culturing long intravascular catheters. *J Hosp Infect* 1989;**14**:183–91.
26 Kite P, Wilcox MH, Dobbins BM, *et al.* Prevalence of endoluminal and extraluminal microorganisms in triple-lumen catheters removed routinely or for suspected sepsis [abstract]. 37th Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, 1997:J57.
27 Widmer AF. IV-related infections. In: Wenzel RP, ed. *Prevention and control of nosocomial infections.* Baltimore: Williams and Wilkins, 1993:556–79.
28 Sitges-Serra A, Linares J. Limitations of semiquantitative method for catheter culture. *J Clin Microbiol* 1988;**26**: 1074–5.
29 Kite P, Dobbins BM, Wilcox MH, *et al.* Evaluation of a novel endoluminal brush for the in-situ diagnosis of catheter related sepsis. *J Clin Pathol* 1997;**50**:278–82.
30 Ryan JA, Abel RM, Abbott WM, *et al.* Catheter complications in total parenteral nutrition; a prospective study of 200 consecutive patients. *N Engl J Med* 1974;**290**:757–61.
31 Padberg FT, Ruggiero J, Blackburn GL, *et al.* Central venous catheterization for parenteral nutrition. *Ann Surg* 1981;**193**:264–70.
32 Cleri DJ, Corrado ML, Seligman SJ. Quantitative culture of intravenous catheters and other intravascular inserts. *J Infect Dis* 1980;**141**:781–6.
33 Sherertz RJ, Heard SO, Raad II. Diagnosis of triple-lumen catheter infection: comparison of roll plate, sonication and flushing methodologies. *J Clin Microbiol* 1997;**35**:641–6.
34 Grabe N, Jakobsen G. Bacterial contamination of subclavian vein catheters: an intraluminal culture method. *J Hosp Infect* 1983;**4**:291–5.
35 Marcus S, Buday S. Culturing indwelling central venous catheters in situ. *Infect Surg* 1989;**8**:157–61.
36 Tighe MJ, Thomas D, Fawley WF, *et al.* An endoluminal brush to detect the infected central venous catheter in situ: a pilot study. *BMJ* 1996;**313**:1528–9.
37 Dobbins BM, Kite P, Wilcox MH, *et al.* Clinical safety of the endoluminal brush technique for in-situ diagnosis of catheter related sepsis [abstract]. 37th Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, 1997:J189.
38 Sitges-Serra A, Linares J, Garau J. Catheter sepsis: the clue is the hub. *Surgery* 1985;**97**:355–7.
39 Segura M, Alvarez-Lerma F, Tellado JM, *et al.* A clinical trial on the prevention of catheter-related sepsis using a new hub model. *Ann Surg* 1996;**223**:363–9.
40 Salzman MB, Isenberg HD, Shapiro JF, *et al.* A prospective study of the catheter hub as a portal of entry for microorganisms causing catheter related sepsis in neonates. *J Infect Dis* 1993;**167**:487–90.
41 Capdevila J, Planes AM, Palomar M, *et al.* Value of differential quantitative blood cultures in the diagnosis of catheter related sepsis. *Eur J Clin Microbiol Infect Dis* 1992;**11**:403–7.
42 Weightman NC, Simpson EM, Speller DCE, *et al.* Bacteraemia related to indwelling central venous catheters: prevention, diagnosis, and treatment. *Eur J Clin Microbiol Infect Dis* 1998;**17**:125–9.
43 Rauncher HS, Hyatt AC, Barzilai A, *et al.* Quantitative blood cultures in the evaluation of septicemia in children with broviac catheters. *J Pediatr* 1984;**104**:29–33.
44 Bjornson HS, Colley R, Bower RH, *et al.* Associations between microorganisms grown at the catheter insertion site and colonisation of the catheter in patients receiving total parenteral nutrition. *Surgery* 1982;**92**:720–7.
45 Fan ST, Teoh-Chan CH, Lau KF, *et al.* Predictive value of surveillance skin and hub cultures in central venous catheter sepsis. *J Hosp Infect* 1998;**12**:191–8.
46 Atela I, Coll P, Rello J, *et al.* Serial surveillance cultures of skin and catheter hub specimens from critically ill patients with central venous catheters: molecular epidemiology of infection and implications for clinical management and research. *J Clin Microbiol* 1997;**35**:1784–90.
47 Cooper GL, Hopkins CC. Rapid diagnosis of intravascular catheter associated infection by direct gram staining of catheter segments. *N Engl J Med* 1985;**312**:1142–7.
48 Coutlee F, Lemieux C, Paradis JF. Value of direct catheter staining in the diagnosis of intravascular-catheter-related infection. *J Clin Microbiol* 1988;**26**:1088–90.
49 Kite P, Tighe MJ, Thomas D, *et al.* Rapid diagnosis of catheter-related sepsis using the acridine orange leucocyte cytospin test and an endoluminal brush. *J Parenter Enter Nutr* 1996;**3**:215–18.
50 Rushforth JA, Hoy CM, Kite P, *et al.* Rapid diagnosis of catheter-related sepsis. *Lancet* 1993;**342**:402–3.
51 Raad I, Costerton W, Sabharwal U, *et al.* Ultrastructural analysis of indwelling vascular catheters: a quantitative relationship between luminal colonization and duration of placement. *J Infect Dis* 1993;**168**:400–7.
52 Pearson ML, Hospital Infection Control Practices Advisory Committee. Guideline for prevention of intravascular-device-related infections. *Infect Control Hosp Epidemiol* 1996;**17**:438–73.
53 Raad I. Intravascular-catheter-related infections. *Lancet* 1998;**351**:893–8.
54 Pearson ML, Abrutyn E. Reducing the risk for catheter-related infection: a new strategy. *Ann Intern Med* 1997;**127**: 304–6.
55 Maki DG, Stolz SM, Wheeler S, *et al.* Prevention of venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. A randomised, controlled trial. *Ann Intern Med* 1997;**127**:257–66.
56 Logghe C, Van Ossel C, D'Hoore W, *et al.* Evaluation of chlorhexidine and silver-sulfadiazine impregnated central venous catheters for the prevention bloodstream infection in leukaemic patients: a randomised, controlled trial. *J Hosp Infect* 1997;**37**:145–56.
57 Ciresi DL, Albrecht RM, Volkers PA, *et al.* Failure of antiseptic bonding to prevent central venous catheter-related infection and sepsis. *Am Surg* 1996;**62**:641–6.
58 Pemberton LB, Ross V, Cuddy P, *et al.* No difference in catheter sepsis between standard and antiseptic central venous catheters. *Arch Surg* 1996;**131**:986–9.
59 Maki DG, Cobb L, Garman JK, *et al.* An attachable silver-impregnated cuff for the prevention of infection with central venous catheters: a prospective, randomised, multicenter trial. *Am J Med* 1988;**85**:307–14.
60 Hasaniya NW, Angelis M, Brown MR, *et al.* Efficacy of subcutaneous silver-impregnated cuffs in preventing central venous catheter infections. *Chest* 1996;**109**:1030–2.
61 Groeger JS, Lucas AB, Coit D, *et al.* A prospective, randomised, evaluation of the effect of silver-impregnated subcutaneous cuffs for preventing tunnelled chronic venous access infections in cancer patients. *Ann Surg* 1993; **218**:206–10.
62 Darouiche R, Raad I, Heard S, *et al.* A prospective, randomized, multicenter clinical trial comparing central venous catheters coated with minocycline and rifampin *vs* chlorhexidine gluconate and silver sulfadiazine [abstract]. 37th Interscience Conference on Antimicrobial Agents and Chemotherapy, Toronto, 1997.
63 Raad I, Darouiche R, Dupuis J, *et al.* Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonisation and bloodstream infections. A randomised, double-blind trial. *Ann Intern Med* 1997;**127**:267–74.
64 Wilcox MH, Kite P, Dobbins B. Antimicrobial intravascular catheters—which surface to coat? *J Hosp Infect* 1998;**38**: 322–4.
65 Faubian WC, Wesley JR, Khaldi N, *et al.* Total parenteral nutrition catheter sepsis: impact of the team approach. *J Parenter Enter Nutr* 1986;**10**:642–5.

66 Elliot TSJ, Moss HA, Tebbs SE, *et al.* Novel approach to investigate a source of microbial contamination of central venous catheters. *Eur J Clin Microbiol Infect Dis* 1997;**16**: 210–13.
67 Livesley MA, Tebbs SE, Moss HA, *et al.* Use of pulsed field gel electrophoresis to determine the source of microbial contamination of central venous catheters. *Eur J Clin Microbiol Infect Dis* 1998;**17**:108–12.
68 Widmer A, Nettleman M, Flint K, *et al.* The clinical impact of culturing central venous catheters. A prospective study. *Arch Intern Med* 1992;**152**:1299–302.
69 Cyna AM, Hovenden JL, Lehmann A, *et al.* Routine replacement of central venous catheters: telephone survey of intensive care units in mainland Britain. *BMJ* 1998;**316**: 1944–5.