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Hemodialysis Access Infections, Epidemiology, Pathogenesis and Prevention

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1. Introduction

Renal replacement therapy (RRT), including various delivery types of haemodialysis, has revolutionised the care of patients with end stage renal disease (ESRD). The most common RRT modality is haemodialysis (ANZ Data 2010, Boddana et al., 2009). Access for dialysis is via arteriovenous fistulae (AVF), arteriovenous grafts (AVG) or via central venous dialysis catheters. The goal of access is to provide a means of accessing the vasculature to undertake RRT in order to deliver the optimal dialysis dose with the minimal associated morbidity and mortality. The National Kidney Foundation (NKF) Kidney Disease Outcome Quality Initiative (KDOQI, 2006) guidelines recommend an AVF prevalence rate of greater than 65%. Arteriovenous fistulae remain the preferred method of access due to improved survival rate and lower associated morbidity and associated medical costs (NKF-KDOQI, 2006). Despite all these measures, dialysis catheters remain commonly used for a variety of reasons. They are now well acknowledged as the harbinger of potential future significant morbidity and mortality.

As a result of the significant morbidity burden caused by dialysis catheters, there has been great interest in discovering new and inventive methods of reducing catheter-related infection. Out of this is borne the investigation of preventative measures outlined here. This is particularly important given the immunosuppressed nature of renal patients. The evidence for, and utility of measures, such as topical antimicrobial ointment application, antimicrobial catheter lock solutions, antibiotic impregnated catheters, differing AVF cannulation methods and catheter design, shall be explored below.

As we strive for improved outcomes in our patients many more patients are undertaking extended hours home haemodialysis. In those patients with the lowest risk accesses, questions have been raised as to the method of access cannulation and the spectre of increasing associated infectious events. The rope ladder technique involves regular rotation of cannulation sites whereas buttonhole technique uses the same cannulation sites and relies on formation of a track which is then repetitively accessed with blunt needles. This has been a very attractive method for home dialysis patients for a range of reasons. However, despite recent popularity with this technique, a number of studies including from our centre, have now shown that this technique is associated with increased septic events (Birchenough et al., 2008; Nesrallah et al., 2010; Van Eps et al., 2010; Van Loon et al., 2010).

2. Vascular access

Vascular access remains a predominant cause of morbidity in haemodialysis patients. There is significant global variation in the use of the different types of haemodialysis access. There have now been a number of studies examining trends of access use (Ethier et al., 2008; Pisoni et al., 2002) and further, epidemiological associations between access type and outcomes (Dhingra et al., 2001; Ishani et al., 2005; Moist et al., 2008; Pastan et al., 2002; Polkinghorne et al., 2004; Xue et al., 2003).

2.1 Geographical and temporal trends in access use

Pisoni et al., (2002) in the Dialysis Outcomes and Practice Patterns Study (DOPPS) confirmed significant variations in access practice between Europe and the United States. The practice comparison found that AVFs were much more common in prevalent patients in Europe, while AVGs and catheters were more commonly used in the US. Arteriovenous fistulae were used in 80% of the European prevalent population compared with only 24% of US prevalent populations and the use was associated with younger male patients with fewer co-morbidities. Use in incident patients varied from 66% in Europe to only 15% in the US. Conversely, AVGs and catheters were more common in incident patients in the US compared to Europe (2% versus 24% and 60% versus 31% respectively). Dialysis catheters were the first modality of access at commencement of dialysis in the US (Pisoni et al., 2002).

Trends in vascular access have changed over time but have shown a progression towards AVF use. Data from DOPPS I (1996-2001), DOPPS II (2002-2004) and DOPPS III (2005-2007) were compared and found that trends towards increasing AVF use were observed in Australia, New Zealand and the United Kingdom. Australia and New Zealand have traditionally had higher rates of AVF use. Arteriovenous fistulae in these countries, along with Japan and most European countries (excluding the United Kingdom, Belgium and Sweden), are used in over 70% of prevalent haemodialysis patients. The use of AVFs had increased significantly in the US in the same time from 24% in DOPPS I to 47% by DOPPS III (Ethier et al., 2008). Most recent data available shows that AVF use in the US is now greater than 57% (www.fistulafirst.org). In all the countries studied, AVG use remained stable or declined. The US showed the greatest decline in prevalent patient use, falling from 58% in DOPPS I to 29% in DOPPS III (Ethier et al., 2008).

Despite efforts to improve outcomes for ESRD patients, dialysis catheters remain a predominant form of vascular access well into the 21st century. Dialysis catheters were observed in greater than 20% of prevalent patients in the UK, Belgium, Sweden, Canada, and the US. A 2- to 3-fold increase in catheter use was observed in Italy, Germany, France and Spain by DOPPS III (Ethier et al., 2008). Catheter use will never be completely eliminated as they have a significant role in those patients who require urgent dialysis and for whom no other access exists. There is often regional variation in access practice patterns. The reasons for this appear to be multifactorial and include variables such as patient preference, surgical wait times, surgical expertise, as well as physician and nursing factors (Polkinghorne, et al., 2004).

2.2 Epidemiological aspects of access type

A number of studies have now shown an epidemiological association between access type and outcome. Use of venous catheters and AVGs over native AVFs has been shown to carry higher human costs. A number of studies have shown an association between catheter use

and increased mortality from both infective and non-infective causes (Dhingra et al., 2001; Pastan et al., 2002; Polkinghorne et al., 2004). One study analysed a random sample of patients from the U.S. Renal Data System Dialysis Morbidity and Mortality Study (USRDS) Wave 1. Both diabetics and non-diabetics with catheters demonstrated similar trends in survival. The best overall survival was observed with AVF over AVG. The poorest survival was seen in patients with catheters (Dhingra et al., 2001). This increased mortality observed with AVGs and catheters has been replicated in a number of studies (Pastan et al., 2002; Polkinghorne et al., 2004; Xue et al., 2003). One of the largest investigations of access-related mortality included over 60,000 patients from the United States (Xue et al., 2003). The use of catheters at iniation of dialysis was associated with the greatest mortality risk (catheter hazard ratio [HR] 1.70, 95% CI 1.59-1.81; AVGs HR 1.16, 95% CI 1.08-1.24; AVF reference). . In this study, greater than 50% of patients commenced dialysis with a catheter.

A *prospective* study of almost 1000 patients in France looked at the risk factors for development of bacteraemia in chronic haemodialysis patients (Hoen et al., 1998). This again confirmed that the greatest risk factor for bacteraemia was use of a dialysis catheter, with an incidence of 0.93 episodes of bacteraemia per 100 patient months. Multivariate analysis confirmed vascular access as a major risk factor for bacteraemia. Catheter use for haemodialysis carried a relative risk of bacteraemia of greater than 7 times that of an AVF (relative risk [RR] 7.6, 95% CI 3.7-15.6). Arteriovenous grafts carried only a marginally higher relative risk compared to AVFs.

Access-related bacteraemia has also been shown to be an important factor in the subsequent development of cardiovascular-related morbidity and mortality. Where cause-specific mortality was assessed, increases in both infectious deaths (Dhingra et al., 2001; Ishani et al., 2005; Pastan et al., 2002; Polkinghorne et al., 2004) and cardiac deaths were also observed (Dhingra et al., 2001; Ishani et al., 2005). Interestingly, in one study, non-diabetics using catheters at the inception of dialysis had a worse survival rate than those patients using permanent vascular access, with the difference being detectable after only 2 months of observation. The overall relative risk of infection-related death was approximately 2-fold higher in patients with central venous catheters over those with AVFs and was more marked in diabetics than non-diabetics. The risk of death from cardiac causes was approximately 1.5-fold higher in those with dialysis catheters (Dhingra et al., 2001). A prospective cohort study of incident dialysis patients in the U.S scrutinised the association between access modality and bacteraemia, and also the association between bacteraemia and cardiovascular events (Ishani et al., 2005). Cox regression analysis (n=2358) demonstrated that initial dialysis access was the main antecedent of septicaemia or bacteraemia. Long term dialysis catheters, temporary dialysis catheters and AVGs displayed HRs of 1.95, 1.76 and 1.05, respectively. The presence of bacteraemia or septicaemia was associated with heightened risks of subsequent cardiovascular morbidity and mortality. In those without defined coronary artery disease, a bacteraemic episode conferred a greater risk of death or acute cardiovascular event than those with pre-existing cardiovascular disease.

A study undertaken in Australia examined incident haemodialysis patients between 1999 and 2002, and made further attempts to statistically adjust for the non-random nature of access selection. This study found that those patients starting dialysis with a dialysis catheter or AVG had a greater risk of dying in the first 6 months compared to those with AVF; catheters being the most life-limiting of all three. This trend continued with time. Dialysing via an AVF showed a mortality rate of 86 per 1000 person-years; AVGs had a

mortality rate of 146 per 1000 person-years and catheters had the highest mortality rate of 261 per 1000 person-years. Catheter use conferred 1.5- to 3-fold increased risks in both infectious and all-cause mortality. A similar trend in both increased infectious and all-cause mortality with AVGs was also observed but not significant on analysis (Polkinghorne et al., 2004).

Apart from catheter-related infectious mortality, proposed alternative mechanisms for the increased death rates in patients with catheters have included reduced dialysis doses delivered by central catheters and a higher prevalence of co-morbid conditions in patients who dialyse via catheters. However, the latter was not confirmed after controlling for vascular disease and congestive cardiac failure (Pastan et al., 2002). No patterns of catheter use associated with increasing age or existing co-morbidities were ascertained from the more recent DOPPS III analysis. The usage of dialysis catheters in younger (18-70 year old) non-diabetics increased 2-fold in the US and up to 3-fold in some European countries (France, Germany, Italy and Spain) (Ethier, et al., 2008).

3. Incidence, pathogenesis and bacteriology of access-related infections

Although the incidence of catheter-related bacteraemia is variable, the mean reported incidence is 3 episodes per 1000 catheter days (Dryden et al., 1991; Moss et al., 1990; Saad, 1999; Mokryzcki et al., 2000; Mokrzycki et al., 2001). Data from the HEMO study (Eknoyan et al., 2008) indicates that patients with central venous catheters have an increased relative mortality risk of 3.4 when compared with patients with AVFs (relative mortality risk of 1.4). The burden of catheter-related infection is high, with reported rates of metastatic infectious complications (e.g. osteomyelitis, endocarditis, septic arthritis or epidural abscess) of between 10% and 40% (Marr et al., 1997; Maya et al., 2007; Neilsen et al., 1998). *S. aureus* is responsible for the majority of vascular access infections, accounting for 70-90% of cases (Del Rio el at., 2009; Gould, 2007).

3.1 Catheter-related bacteraemia

Gram-positive species are the culprit organisms in 61-95% of cases of catheter-related bacteraemia. In the prospective study by Hoen et al (1998), the most common causative organism was *S. aureus*. Coagulase-negative staphylococcal bacteraemia was almost as common as that caused by *S. aureus*. *Escherichia coli* and other aerobic gram negative bacilli were the next most commonly isolated organisms. The presumed portal of entry for these organisms was via the vascular access. In this study, 6 deaths were directly attributable to bacteraemia. The most common causative organisms under these circumstances were *S. aureus* and *Pseudomona*s with equal occurrence, and other Enterobacteriaciae making up the remainder of isolated agents (Hoen et al., 1998).

Catheter-related bacteraemia may arise via two paths: (a) direct spread of microorganisms from the skin along the outside of the catheter leading to contamination of the bloodstream; or, (b) colonisation of the inner lumen of the catheter leading to the formation of biofilm and direct migration of organisms into the bloodstream. A biofilm is a multi-layered cell cluster with a strong propensity to adhere to polymer surfaces and provides a protected niche environment for microorganisms with physical barrier protection against antibiotics. Within the biofilm, bacteria exhibit increased growth rates, a higher cell density and more active gene transcription. This further contributes to the heightened resistance of bacteria to antibiosis (Fux et al., 2003). Even in the absence of

overt infection, microbial colonisation of catheters may engender a chronic inflammatory state, which in turn increases the risk of erythropoietin-resistant anaemia, malnutrition and cardiovascular disease (Barraclough et al., 2009).

3.2 Arterio-venous fistula bacteraemia

In those with AVF infection, *S. aureus* and *Staphylococcus epidermis* are most commonly responsible. Infection accounts for approximately one fifth of accesses being lost (Bhat et al., 1980). Microorganisms gain entry to the bloodstream during cannulation. In addition, the presence of pseudoaneuryms, peri-access haematomas, non-functioning clotted fistulae and manipulation of AVFs during non-dialysis interventions increase the risk of infection (Barraclough et al., 2009).

Recent evidence suggests that cannulation technique may have an important effect on the rates of bacteraemia related to AVFs. Over the last 30 years, the buttonhole cannulation technique has become increasingly popular. This technique involves repetitive cannulation of a small number of puncture sites, with the aim of creating a tunnel track into which the needles can be easily inserted. There are a number of benefits associated with using buttonhole cannulation for haemodialysis, particularly in the home environment. These benefits include easier and quicker needle insertion, less painful cannulation with the elimination of anaesthetic, reduction in "bad sticks", and reduction in hematoma formation (Doss et al., 2008; Hartig and Smyth, 2009). The alternative cannulation method, referred to as the rope ladder technique, involves needle puncture along the length of the fistula and is more inclined to give rise to small dilatations over the length of the fistula. However, several studies have suggested that the buttonhole technique is associated with an increased risk of access-related infection compared with the rope ladder method. Birchenough et al. (2008) established a positive correlation between use of the buttonhole cannulation technique and an increased risk for infection in adult patients on haemodialysis. Nesrallah et al. (2010) observed a significantly increased risk of *S. aureus* bacteremia infection with potentially fatal metastatic complications in patients receiving home nocturnal haemodialysis with buttonhole cannulation. They recommended advising prospective patients of the infection risks, and, in the absence of more rigorous studies, giving consideration to topical Mupirocin prophylaxis. Other studies have similarly reported increased access-related infection rates in association with buttonhole cannulation (Ludlow, 2010; Silva et al., 2010; Van Loon et al., 2010).

A subsequent retrospective observational cohort study in our unit involving 63 alternate nightly nocturnal haemodialysis and 172 conventional haemodialysis patients reported a statistically significant and clinically important increase in septic dialysis access events when nocturnal haemodialysis and buttonhole cannulation were used simultaneously (incidence rate ratio 3.0, 95% CI 1.04-8.66, p=0.04) (Van Eps et al., 2010). It is theorised that chronic bacterial colonisation of the buttonhole site may be the precursor to systemic infection, and that fibrosis surrounding the site may not provide as efficient a barrier as seen in those employing the rope ladder technique. This study highlights that increased infection control steps may be crucial in the setting of nocturnal haemodialysis and buttonhole technique.

4. Preventative measures against access-related infection

4.1 Aseptic technique

The method of handling the dialysis catheter is crucial. Stringent aseptic techniques must be employed, with KDOQI 2006 recommending washing the access site with antibacterial scrub and water followed by cleansing of the skin with 2% chlorhexidine/alcohol or 70% alcohol.

A multicentre prospective randomised trial (n=849) compared chlorhexidine-alcohol with povidone-iodine in the setting of post-operative surgical wounds and found that the chlorhexidine-alcohol preparation was associated with a significantly lower rate of surgical site infection (9.5% vs 16.1%, p=0.004, RR 0.59, 95% CI 0.41 – 0.85). However, in dialysis populations, there are only a few RCTs detailing the value of different antiseptic ointments. A small RCT studying povidone-iodine in subclavian catheters demonstrated a statistically significant improvement in exit site infections (5% vs 18%, p<0.02), tip colonisations and incidence of septicaemia compared with using sterile gauze dressings alone in the control group (Levin et al., 1991). The beneficial effect of povidone-iodine ointment was most marked in those with *S. aureus* nasal carriage (3-fold higher risk of subclavian catheter-related septicaemia, p<0.05). No significant increase in adverse effects was observed with povidone-iodine.

There is no particular dressing type that has shown benefit over another. A chlorhexidine-impregnated foam dressing has not been found to provide extra protection against infection in an open labelled study (Camins et al., 2010), despite previous evidence to the contrary in patients in an intensive care setting (Timsit et al., 2009).

Maximal sterile barrier precautions were further studied in a recent Korean study. Using multivariate analyses, they found that the use of maximally sterile barrier precautions (odds ratio 5.205 95% CI 0.015 – 1.130, p=0.23) and use of antimicrobial coated catheters (odds ratio 5.269 95% CI 0.073 – 0.814, p=0.022) were independent factors associated with a lower risk of acquiring a central venous catheter-related bacteraemic episode (Lee at al., 2008). In another single centre study, the institution of a catheter monitoring system and a formal maintenance program following catheter insertion was associated with a reduction in the occurrence of catheter-related bacteraemia by 33% (Yoo et al., 2001). A Cochrane systematic review of randomised controlled trials (McCann and Moore, 2010) reported that transparent polyurethane dressing did not reduce the risk of catheter-related exit site infection or bacteraemia compared to dry gauze.

4.2 Catheter care protocols

It is well accepted practice in the critical care sector to adopt a strictly protocolised approach to the care of central venous catheters (Beathard and Urbanes, 2008; Pronovost et al., 2010). Care bundles are commonly used in the intensive care unit. A "care bundle" is a set of evidence-based interventions that are administered to many intensive care patients, with the aim of risk reduction. There is no randomised trial evidence in the haemodialysis population, but prospective observational data has shown a marked reduction in bacteraemic episodes from 6.7 to 1.6 per 1000 catheter days over a twenty four month study period using an infection prophylaxis protocol based on NKF-K/DOQI guidelines (2001). The main focus of the protocol was strict cleansing of the catheter hub at the time of use in the dialysis facility to avoid any potential contamination. Other vital elements to catheter care include the technical placement of the catheter, exit site care and the handling of dialysis connections.

4.3 Topical antimicrobial agents

Use of topical antimicrobial agents has been associated with reduced rates of bacteraemic episodes and catheter loss of any cause (Rabindranath et al., 2009). Our group was one of the first to demonstrate that topical exit site application of mupirocin, an antibiotic active against Gram-positive organisms, resulted in significantly fewer catheter-related

bacteraemias (7 vs 35%, p<0.01) and a longer time to first bacteraemia (log rank score 8.68, P<0.01) (Johnson et al., 2002). The beneficial effect of mupirocin was entirely attributable to a reduction in staphylococcal infection (log rank 10.69, P=0.001) and was still observed when only patients without prior nasal *S. aureus* carriage were included in the analysis (log rank score 6.33, P=0.01). Median catheter survival was also significantly longer in the mupirocin group (108 vs 31 days, log rank score 5.9, P<0.05).

Recently, McCann & Moore (2010) published the results of their Cochrane systematic review in which they evaluated the benefits and harms of prophylactic topical antimicrobial agents on infectious complications among haemodialysis patients with central venous catheters. In a total of 10 randomised controlled trials involving 787 patients, the risk of catheter-related bacteraemia was reduced by topical exit site application of mupirocin (RR 0.17, 95%CI 0.07 - 0.43), polysporin triple ointment consisting of bacitracin, gramicidin and polymixin B (RR 0.40, 95% CI 0.19 – 0.86), and povidone-iodine ointment (RR 0.10, 95% CI 0.01 – 0.72). Mortalityrelated to infection was not reduced by any of these three agents.

In another meta-analysis topical antimicrobial agents reduced the rates of bacteraemia (risk rate ratio 0.22, 95% CI 0.12 – 0.40), exit site infection (RR 0.17, 95% CI 0.08 – 0.38), requirement for catheter removal and hospitalisation for infection compared with no antibiotics (James et al., 2008).

In spite of the demonstrated benefits of topical antimicrobial agents on catheter-associated infection rates, a real concern surrounding these agents is the potential risk of antibiotic resistance. Whilst these fears have not yet been realised, a number of groups have suggested that antimicrobial prophylactic therapy should be limited in duration and scope to minimise the possibility of promoting antimicrobial resistance. For example, a recent position statement issued by the European Renal Best Practice (ERBP) working group recommended the application of antimicrobial ointments (either mupirocin or polysporin ointment) after catheter placement only until the exit site has healed completely (Tordoir et al., 2007). They specifically advised against the use of these agents after the site has healed because of the fear of emerging resistance and *Candida* colonisation.

4.4 Antimicrobial locks

There is evidence that "locking" a catheter with a small amount of antimicrobial agent that remains within the catheter lumen can prevent bacteraemic episodes. These antimicrobial locks are thought to possess extra biofilm-removing properties. This is in contrast to heparin, which may serve to antagonise the antibacterial properties of certain antibiotics (Droste et al., 2003, Regamey et al., 1972) and may in fact promote biofilm formation (Shanks et al., 2006).

Nine randomised controlled trials looked at the potential role of antimicrobial locks versus the standard heparin lock. The mean baseline risk of catheter-related infection was 3.0 episodes per 1000 catheter days, with the catheter insertion duration ranging from 37-365 days (mean 146 days). Seven out of 9 trials used an antibiotic, 1 used taurolidine and 1 used 30% citrate. The different antimicrobial preparations included amikacin, cefazolin, cefotaxime, ciprofloxacin, EDTA, gentamicin, minocycline and vancomycin. Collectively, they showed a more than three-fold reduction in the occurrence of catheter-related bacteraemia, in addition to reductions in mortality and morbidity (Allon et al., 2008; Jaffer et al., 2008; Labriola et al., 2008;). Seven out of 9 of the studies reached statistical significance. The use of antimicrobial locks also significantly reduced the rate of catheter loss due to all complications (3 trials; n=399; RR 0.61, 95% CI 0.45-0.83) (Rabrinathan et al., 2009).

Unfortunately, most of these trials were of short duration, being limited to 12 months follow-up or less. Consequently, the long-term risk:benefit of antimicrobial locks is uncertain. Significant side effects of antimicrobial locks that have been documented in the above trials included hypocalcaemia (Power et al., 2009) digital parasthesiae (Power et al., 2009) and ototoxicity in 10% of those using gentamicin based catheter locks (Dogra et al., 2002). Moreover, there are significant concerns that long term use of antimicrobial locks may promote multiresistant organisms (MROs). An American unit using a gentamicin/heparin lock observed the appearance of gentamicin resistant bacteraemia after a period of 6 months (Landry et al., 2010). The most common complications following such bacteraemias were catheter removal and hospital admission. Thus, despite a 95% decrease in the rate of catheter-related bacteraemia, there was the emergence of gentamicin resistant gram negative infections with tunnelled catheters being the most common access in the group. After stopping the gentamicin antimicrobial lock, the resistance to gentamicin dropped after 18 months.

4.5 Non-antimicrobial locks
4.5.1 Citrate
The spectre of antibiotic resistance has led nephrologists to seek alternative catheter lock agents. Sodium citrate has been utilised as an alternative anticoagulant to intradialytic heparin. Anticoagulant activity is brought about by reducing the free plasma calcium concentration and thus retarding the coagulation cascade. A 30% citrate solution will have antimicrobial and antibacterial properties. Citrate does not promote bacterial resistance and therefore has been proposed as the ideal catheter lock solution (Bleyer, 2007).

Power et al. (2009) studied 232 haemodialysis patients randomised to either 46.7% sodium citrate or 5% heparin locks post-dialysis for a 6 month period. In both groups, the rate of catheter-related bacteraemia was 0.7 events per 1000 catheter days with no significant difference between groups. There was a statistically significant increase in catheter thrombosis in the citrate group (p<0.001). All patients had a tunnelled twin catheter single lumen Tesio catheter.

Weijiner et al. (2005) had previously shown an added benefit of Trisodium citrate 30% in a randomised controlled trial incorporating 291 randomised haemodialysis patients. In this group however, 98/291 (34%) and 193/291 (66%) possessed tunnelled cuffed catheters and non-tunnelled catheters respectively. Catheter-related infection rates were 1.1 per 1000 catheter days in the trisodium citrate 30% group versus 4.1 per 1000 in the heparin group (p<0.001). There was found to be no difference in the rate of thrombotic events. This study showed a risk reduction for catheter-related bacteraemia of 87% for tunnelled catheters (p<0.001) and 64% for non-tunnelled catheters (p=0.05). There were fewer deaths from bacteraemia in the trisodium citrate 30% group (0 vs 5, p=0.028). Exit site infections were also reduced.

A concern with use of citrate relates to its chelating properties that can lead to hypocalcaemia with subsequent risk of ventricular arrhythmias. The death of a patient in 2000 from cardiac arrest following installation of 46.7% sodium citrate into a haemodialysis catheter prompted a Food and Drug Association (FDA) warning about its use (Food and Drug Administration, 2009). Many haemodialysis centres therefore avoid high doses of citrate in catheter locks. There is ongoing interest in using lower concentrations of sodium citrate, either alone or in combination with taurolidine or ethanol.

4.5.2 Taurolidine

Taurolidine locks possess antimicrobial activity by producing methyl taurinamde products that bind to bacterial and fungal cell walls and cause damage. The antimicrobial effect is broad spectrum and has been shown to reduce the progression to biofilm production (Torres-Viena et al., 2000). There are no reports of antibiotic resistance.

A randomised controlled trial from the United Kingdom randomised subjects to receive either Taurolidine-Citrate lock (1.35% taurolidine & 4% citrate) or unfractionated heparin 5000units/mL. The primary outcome was time to first bacteraemic episode and secondary outcomes were total number of bacteraemic episodes and gram positive and gram negative infections. There was found to be no statistically significant difference in time to first bacteraemic episode (n=110). However, there was a significant reduction in gram negative infections (p=0.02). The main drawback to using Taurolidine-citrate locks is a greater need for thrombolytic therapy. Solomon et al. (2010) surmised that tauroldine-citrate usage impacted only infection of intraluminal origin and that better formulations with an improved anticoagulant profile should be sought. These findings echo those trends seen previously (Allon, 2003, Betjes and Van Agteren 2004; Taylor et al., 2008).

4.5.3 Ethanol

Ethanol is an effective disinfectant with a broad spectrum of activity against a host of micro-organisms. Its benefits include low toxicity, lack of antibiotic resistance, ready availability and low cost. Ethanol-containing catheter locks were initially used in oncology patients to maintain long term catheters and in those receiving total parenteral nutrition in order to manage catheter occlusion (Ball et al., 2003; Metcalf et al., 2004; Pennington and Pithie, 1987). As little as 60 minutes exposure to a 30% ethanol- 14% trisodium citrate locking solution has been show to effectively eradicate the common gram-positive and gram-negative bacteria colonising catheters (Takla et al., 2007). Maharaj et al. (2008) demonstrated an equally impressive effect on *Candida albicans* isolates within the same time frame. These antimicrobial benefits of ethanol appear to be associated with a neutral effect on the integrity of catheter material. A recent small study tested found no negative effect of a 30% ethanol-4% sodium citrate locking solution on catheters (Vercaigne et al., 2010). Guenu et al. (2007) similarly found no deterioration in silicone catheter viability following exposure to high concentrations of ethanol.

Our unit is currently conducting a randomised controlled trial of heparin versus ethanol lock for the prevention of catheter-associated infection (Broom et al., 2009). This is a single centre prospective open-label study comparing 3mL 70% ethanol catheter lock head to head with a standard heparin lock. Using time to first catheter-related bacteraemia as the primary outcome, the study will hopefully elucidate further the benefit of ethanol as a useful preventative measure against catheter-related infections.

4.5.4 Honey

The healing properties of honey have been recognised since antiquity. Ancient Greeks and Egyptians used honey to aid in the healing of burns and sores. During World Ward I German physicians used honey and cod liver oil together as a surgical dressing for battle wounds. The antimicrobial properties of honey are related to its very high sugar content, which kills bacteria through dessication, and enzymatic production of hydrogen peroxide (glucose + H_2O + O_2 → gluconic acids + H_2O_2). The enzyme glucose oxidase also confers

acidity to the substance. The pH range of honey is 3.2-4.5, which is low enough to be inhibitory to many bacterial pathogens. Moreover, research has shown that peripheral B lymphocytes and T lymphocytes proliferate in the presence of honey concentrations as low as 0.1%, and that phagocytes are activated by honey at these same low concentrations (Abbas, 1997). Our unit has succeeded in showing the advantageous effects of Medihoney in a randomised controlled trial comparing thrice weekly exit site application of standardised antibacterial honey versus 2% mupirocin ointment on infection rates in patients with cuffed tunnelled central venous catheters (Johnson et al., 2005). Topical Medihoney led to comparable rates of catheter-related infection compared to those achieved with mupirocin, but conferred additional benefits including low cost, an excellent safety profile and lack of antibiotic resistance, especially mupirocin resistance.

4.6 Nasal eradication of *S. aureus*

Historically, nasal carriage of *S. aureus* has been associated with greater bacteraemic episodes with *S. aureus* in haemodialysis patients (Yu et al., 1986). Patients on chronic haemodialysis have been reported to have over twice the rate of *S. aureus* nasal colonisation as healthy controls. More recent data are in agreement with this, and it is widely believed that nasal colonisation provides a natural reservoir that facilitates ongoing habitation and propagation of *S. aureus* in human populations. (Elie-Turenne et al., 2010; Mermel et al., 2010). Nasal application of mupirocin has been proven to eradicate nasal carriage of *S.aureus* in up to 98.5% of cases (Taal et al., 2006). This strategy has been associated with a reduction in *S. aureus* bacteraemia compared to historical controls (Boelart et al., 1993), although again, use has been associated with the development of mupirocin resistance (Cavdar et al., 2004; Lobbedez et al., 2004). Currently however, there are no recommendations by the leading Nephrology bodies to perform routine eradication of nasal *S.aureus* in a bid to reduce catheter-related bacteraemia.

4.7 The role of catheter design, structure and placement

The first 30 days following catheter placement are vital to the prevention of bloodstream infection. During this period, technique should not be compromised as the main risk of entry is infection through medical staff interaction and the patient's normal skin microflora. After this time, the catheter is more vulnerable to internal sources of infection, possibly via the catheter hub, leading to subsequent haematogenous spread and bloodstream infection. Alternatively, infection at a distant internal site may lead to colonisation of the indwelling catheter (Knuttinen et al., 2009).

4.7.1 Tunnelled versus non-tunnelled catheters

The incidence of bacteraemia is greatly reduced in subjects using cuffed tunnelled catheters as opposed to non cuffed catheters. The majority of modern cuffed tunnelled catheters are made of either polyurethane or silicone. The cuffed portion, which lies in the subcutaneous tissue near the insertion site, creates a fibrous seal and provides an effective barrier against infection by preventing migration of bacteria down the outer surface of the catheter. Although there are no prospective randomised trials investigating infection-related morbidity between catheter types in the dialysis population, observed bacteraemia rates range from 0.16–0.86 per 100 days with non-tunnelled non-cuffed dialysis catheter to 0.016–0.27 per 100 days with tunnelled cuffed catheters. Evidence from the non-haemodialysis setting showed lower infection rates in tunnelled catheters (Andrivet et al., 1994; Timsit et

al., 2007). Within a set of immunocompromised patients, the rates of bacteraemia were reduced by cuffed catheters (2% vs 5%), although this did not achieve statistical significance (Andrivet et al., 1994).

There is no clear evidence pointing to any differences in bacteraemia rates attained through usage of different catheter brands. Some groups have published data of long term tunnelled catheter usage (Tesio catheters, MedComp, Harleysville, Pennsylvania) highlighting bacteraemia rates similar to those achieved in arteriovenous fistulae. This particular group utilised strict protocols surrounding catheter care (Power et al., 2011). The four most commonly commercially available tunnelled catheters are the HemoSplit, Tesio twin catheter, Split-Catheter III and Permcath. A UK study examining catheter survival found that the Split Catheter III and Permcath fared worse than the HemoSplit and Tesio twin catheter. Infection rates were not specifically studied (Fry et al., 2008).

4.7.2 Catheter placement

There is no randomised trial evidence of any specific site of insertion conferring an increased risk of infection (Ruesch et al., 2002). In a large study of intensive care patients there was no statistically significant difference in the incidence of infection or duration of catheter amongst the insertion sites (Deshpande et al., 2005). Multivariate analyses from a number of studies have collectively suggested a higher rate of infection with the femoral vein location, with the infection risk with the jugular approach being greater than the subclavian approach (Breschan et al., 2007; Ishizuka et al., 2009, Ishizuka et al., 2008; Nagashima et al., 2006). These studies did not take into account baseline confounding variables.

4.7.3 Catheter devices

Trerotola et al.(2010) found no improvement in infection rates in tunnelled small bore central venous catheters with the insertion of a polyester cuff.

4.7.4 Antibiotic-impregnated catheters

Since the early 1990's, there have been different types of central venous catheter antibiotic coatings trialled primarily in the critical care setting. There are no RCTs of antibiotic impregnated catheters in the chronic haemodialysis population. Raad et al. (1997) compared minocycline and rifampicin coated catheters head to head with untreated uncoated catheters, and found a significantly reduced rate of catheter related bacteraemia (0% versus 5%, respectively). This was a double blinded study (n=281) where the antibiotic coated catheters had been pre-treated with tri-idodecyclmethylammoniumchloride surfactant. The minocycline and rifampicin components were both active against methicillin-sensitive and methicillin-resistant *S. aureus*, and also had reported activity against gram negative bacilli and *Candida* species. Within a multicentre study of intensive care units, Maki et al. (1997) found a higher degree of bacterial colonisation of the catheter material in the uncoated as compared to the antibiotic impregnated catheters.

Following these results, the United States CDC recommended the use of antibiotic coated catheters for those with a high rate of infection after full adherence to other infection control measures, such as maximal sterile barrier precautions. There was also a recommendation that in an adult with an expected need for a central venous catheter for more than five days an antibiotic impregnated catheter be used in preference.

More recently, a large retrospective study of central venous catheters in the critical care setting showed that there was a significant reduced incidence of catheter-related infection that was independent and complementary to the infection control precautions utilised. The incidence improved from 8.3 episodes of infection per 1000 patient days to 1.2 episodes per 100 patient days (Ramos et al., 2010). The body of evidence refers to only non-cuffed non-tunnelled catheters, and has not led to the wide availability of such devices in the chronic haemodialysis population.

4.8 Thrombolytic therapy

Catheter-related bacteraemia may arise via the formation of an intraluminal thrombosis, which may then act as a nidus for the development of bacterial biofilm (McGee et al., 2003; Jain et al., 2009). Recombinant tissue plasminogen activator has been shown to be useful in catheter thrombus (Clase et al., 2001; Macrae et al., 2005; Tumlin et al., 2010) and some paediatric studies have looked into its potential effect on bacteraemia rates in the haemodialysis population. It has been shown that the prophylactic use of a catheter lock containing tissue plasminogen activator plus antibiotic can reduce the incidence of catheter–related bacteraemia, and may improve the infection-free survival times of central catheters at high risk of infection (Onder et al., 2009).

4.9 Aspirin

In vitro and in vivo animal studies of infective endocarditis have demonstrated aspirin to have direct anti-staphylococcus effects. It is theorised that the salicylic component of aspirin, which is the major biometabolite, inhibits the expression of two key *S. aureus* virulence genes involved in endovascular pathogenesis. A retrospective observational study over 10 years in a single haemodialysis centre found a lower rate of catheter-associated *S. aureus* bacteraemia in patients using aspirin at a daily dose of 325mg (Sedlacek et al., 2007).

5. Conclusions

The goal of treatment of patients with end-stage kidney failure is to provide optimal dialysis while at the same time averting excess morbidity and mortality. It should always be borne in mind that this patient group is a vulnerable and relatively immunosuppressed cohort, often with appreciably significant co-morbidity. Evidence points towards the best outcome being achieved when dialysis is initiated using a native arteriovenous fistula, with the next best outcome with an arteriovenous graft. However, concomitant disease burden can make native access formation challenging.

The use of central venous catheters for dialysis purposes should be minimised and actively discouraged (ERBP Guidelines 2007, KDOQI 2006, CARI 2000) as they are associated with increased patient mortality, morbidity and cost of healthcare. The consequences of catheter-related bacteraemia may be life-threatening, and could reach a 10% mortality rate (Saxena et al., 2002) and also effect cardiovascular morbidity. For those individuals where haemodialysis catheters are hard to avoid, a proactive approach is appropriate, and various preventative measures should be considered. The use of a catheter care protocol may be beneficial. The concept of the "care bundle" may be an extremely useful tool in the haemodialysis environment. In many ways the dialysis patient often has multi-organ involvement and a stepwise, astringent, highly protocolised pathway is appropriate.

Institution of such protocols has resulted in a drastic reduction in catheter-related bacteraemia reported in some American intensive care units (Pronovost et al., 2006).

The use of antibiotic lock solutions and topical antimicrobial ointment (mupirocin, povidone-iodine and polysporin triple antibiotic) has been shown to be effective in reducing bacteraemia. The benefits of citrate locks have been demonstrated by two meta-analyses (Yahav et al., 2008; Labriola et al., 2008). However, there are tenable concerns regarding cardiac arrhythmias, which may be circumvented by using lower concentrations of citrate that may compromise their antimicrobial potency. Topical medical-grade honey has proved efficacious against exit site infection. Prophylactic antibiotic at the time of insertion is frequently administered, although this intervention has never been validated in randomised controlled trials (Ryan et al., 2004).

Antibiotic coatings are in wide usage in the critical care arena using non-cuffed non-tunnelled catheters, but their usage has not crossed over to the dialysis unit. Novel therapies, such as thrombolytic agents and aspirin, require larger randomised studies before their widespread use is advocated.

We now have an increasing number of possible interventions in our armentarium to help us offer the best care to our patients. However, much more evidence in the form of clinical trials is needed to further elucidate the efficacy of these preventative measures, and other potential treatments.

6. References

Abbas T. *(*1997) Royal treat. *Living in the Gulf*; 50-1.

Allon M. *(*2003). Prophylaxis against dialysis catheter related bacteraemia with a novel antimicrobial lock solution. *Clinical Infectious Disease*; 36: 1539-1544.

Allon M. (2008). Prophylaxis against dialysis catheter-related bacteraemia: a glimmer of hope. *American Journal of   Kidney Disease*; 51: 165–168.

Andrivet P, Bacquer A, Ngoc CV & Ferme C. (1994). Lack of clinical benefit from subcutaneous tunnel insertion of central venous catheters in immunocompromised patients. *Clinical Infectious Diseases*; 18(2): 199-206.

ANZDATA Registry 2010 Report. (2010). The thirty third report. http://www.anzdata.org.au/anzdata/AnzdataReport/33rdReport/ANZDATA33 rdReport.pdf

Ball PA, Brokenshire E, Parry B, Merrie A, Gillanders L, McIlroy K & Plank L. (2003). Ethanol locking as a possible treatment for microbial contamination of long-term central venous catheters. *Nutrition*; 19 (6): 570

Barraclough KA, Hawley CM, Playford EG & Johnson DW. (2009). Prevention of access-related infections. *Expert   Reviews in Anti-Infective Therapy*; 7(10): 1185-200.

Beathard GA & Urbanes A. (2008). Infection associated with tunnelled haemodialysis catheters. *Seminars in Dialysis*; 21: 521-538.

Betjes MGH & Van Agteren M. *(*2004). Prevention of dialysis catheter-related sepsis with a citrate-taurolidine-containing lock solution. *Nephrology Dialysis Transplantation;* 19: 1546-1551.

Bhat DJ, Tellis VA, Kohlberg WI, Driscoll B & Veith FJ. (1980). Management of sepsis involving expanded polytetrafluoroethylene grafts for haemodialysis access. *Surgery*; 87(4): 445-50.

Birchenough E, Moore C, Stevens K, & Stewart S. (2010). Buttonhole cannulation in adult patients on haemodialysis: an increased risk of infection? *Nephrology Nursing Journal*; 37(5): 491-555.

Bleyer AJ. (2007). Use of antimicrobial catheter lock solutions to prevent catheter-related bacteraemia. *Clinical Journal of the American Society of Nephrology*; 2(5): 1073-1078.

Boddana P, Caskey F, Casula A & Ansell D. (2009). UK Renal Registry 11th Annual Report (December 2008): Chapter 14 UK Renal Registry and international comparisons. *Nephron Clinical Practice;*, 111 Suppl 1: c269-76.

Boelaert JR, Van Landuyt HW, Godard CA Daneels RF, Schurgers ML, Matthys EG, De Baere YA, Gheyle DW, Gordts BZ & Herwaldt LA. (1993). Nasal mupirocin ointment decreases the incidence of *Staphylococcus aureus* bacteraemias in haemodialysis patients. *Nephrology Dialysis Transplantation*; 8(3): 235-239.

Breschan C, Platzer M, Jost R, Schaumberger F, Stettner H & Likar R. (2007). Comparison of catheter-related infection and tip colonization between internal jugular and subclavian central venous catheters in surgical neonates. *Anesthesiology*; 107(6): 946–53.

Broom JK, O'Shea S, Govindarajulu S, Playford G, Hawley CM, Isbel NM, Campbell SB, Mudge DW, Carpenter S, Johnson BC, Underwood N & Johnson DW (2009). Rationale and design of the HEALTHY-CATH trial: A randomised controlled trial of Heparin versus EthAnol Lock THerapY for the prevention of Catheter Associated infecTion in Haemodialysis patients. *BMC Nephrology*; 10: 23

Camins BC, Richmond AM, Dyer KL & Zimmerman HN. (2010). A crossover intervention trial evaluating the efficacy of a chlorhexidine-impregnated sponge in reducing catheter-related bloodstream infections among patients undergoing haemodialysis. *Infection Control and Hospital Epidemio*logy; 31(11): 1118-23.

CARI *(Caring for Australasians with Renal Impairment) Guidelines. (2000). Dialysis Guidelines: Vascular Access.* Available at www.cari.org.au

Cavdar C, Atay T, Zeybel M, Celik A, Ozder A, Yildiz S, Gulay Z & Camsari T. (2004). Emergence of resistance in staphylococci after long-term mupirocin application in patients on continuous ambulatory peritoneal dialysis. *Advances in Peritoneal Dialysis*; 20: 67-70.

Clase CM, Crowther MA, Ingram AJ & Cina CS. (2001). Thrombolysis for restoration of patency to haemodialysis central venous catheters: a systemic review. *Journal of Thrombosis and Thrombolysis*; 11: 127-36.

Del Rio A, Cervera C, Moreno A, Moreillon P & Miro JM. (2009). Patients at risk of complications of *Staphylococcus aureus* bloodstream infection. *Clinical Infectious Disease*; 48(4): S246–S253.

Deshpande KS, Hatem C, Ulrich HL & Currie BP. (2005). The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Critical Care Medicine*; 33: 13–20.

Dhingra RK, Young EW, Hulbert-Shearon TE, Leavey SF & Port FK. (2001). Type of vascular access and mortality in US haemodialysis patients. *Kidney International* 2001; 60(4): 1443–51.

Dogra GK, Herson H, Hutchison B, Irish AB, Heath CH, Golledge C, Luxton G & Moody H. (2002) . Prevention of tunnelled haemodialysis catheter-related infections using catheter-restricted filling with gentamicin and citrate: a randomized controlled study. *Journal of the American Society of Nephrology*; 13(8): 2133-9.

Doss S, Schiller B, Moran J. (2008). Buttonhole cannulation – an unexpected outcome. *Nephrology Nursing Journal*; 35(4): 417-419.

Droste JC, Jeraj HA, MacDonald A & Farrington K. (2003). Stability and in vitro efficacy of antibiotic-heparin lock solutions potentially useful for treatment of central venous catheter-related sepsis. *Journal of Antimicrobial Chemotherapy*; 51: 849–855.

Dryden MS, Samson A, Ludlam HA, Wing AJ & Phillips I. (1991). Infective complications associated with the use of Quinton Permcath for long-term central vascular access in haemodialysis. *Journal of Hospital Infection*; 19: 257–262.

Eknoyan G, Beck GH, Cheung AK, Daugirdas JT, Greene T, Kusek JW, Allon M, Bailey J, Delmez JA, Depner TA, Dwyer JT, Levey AS, Levin NW, Milford E, Ornt DB, Rocco MV, Schulman G, Schwab SJ, Teehan BP & Toto R; Hemodialysis (HEMO) Study Group. (2002). Effect of dialysis dose and membrane flux in maintenance haemodialysis. *New England Journal of Medicine*; 347: 2010–2019.

Elie-Turenne MC, Fernandes H, Mediavilla JR, Rosenthal M, Mathema B, Singh A, Cohen TR, Pawar KA, Shahidi H, Kreiswirth BN, & Deitch EA. (2010). Prevalence and characteristics of *Staphylococcus aureus* colonization among healthcare professionals in an urban teaching hospital. *Infection Control and Hospital Epidemiology*; 31: 574–580.

Ethier J, Mendelssohn DC, Elder SJ, Hasegawa T, Akizawa T, Akiba T, Canaud BJ & Pisoni RL. (2008). Vascular access use and outcomes: an international perspective from the dialysis outcomes and practice patterns study. *Nephrology Dialysis Transplantation*; 23: 3219–3226.

Fistula First Breakthrough Initiative (FFBI). (2007). Summary of the FFBI buttonhole technique environmental scan. http://www.fistulafirst.org.

Fry AC, Stratton J, Farrington K & Mahna K. (2008). Factors affecting long-term survival of tunnelled haemodialysis catheters—a prospective audit of 812 tunnelled catheters. *Nephrology Dialysis Transplantation*; 23(1): 275-281.

Fux CA, Stoodley P, Hall-Stoodley L & Costerton JW. (2003). Bacterial biofilms: a diagnostic and therapeutic challenge. *Expert Reviews in Anti-Infective Therapy*; 1: 667–683.

Gould IM. (2007). MRSA bacteraemia. *International Journal of Antimicrobial Agents*; 30(Suppl 1): S66–S70.

Guenu S, Heng AE, Charbonne F, Galmier MJ, Charles F, Deteix, Souweine B & Lartigue C. (2007). Mass spectrometry and scanning electron microscopy study of silicone tunnelled dialysis catheter integrity after an exposure of 15 days to 60% ethanol solution. *Rapid Commununications in Mass Spectrometry*; 21:229-236.

Hartig V & Smyth W. (2009). Everyone should buttonhole: a novel technique for a regional Australian renal service. *Journal of Renal Care*; 35(3): 114-9.

Hoen B, Paul-Dauphin A, Hestin D & Kessler M. (1998). *EPIBACDIAL: a multicenter prospective study of risk factors for bactaeremia in chronic haemodialysis patients.* Journal of the American Society of Nephrology; 9: 869-876.

Ishani R, Collins AJ, Herzog C & Foley R. (2005). Septicaemia, access and cardiovascular disease in dialysis patients: The USRDS Wave 2 Study. *Kidney International*; 68: 311–318.

Ishizuka M, Nagata H, Takagi K & Kubota K. (2009). Femoral venous catheterization is a major risk factor for central venous catheter-related bloodstream infection. *Journal of Investigative Surgery*; 22: 16–21.

Ishizuka M, Nagata H, Takagi K, Horie T, Furihata M, Nakagawa A & Kubota K. (2008). External jugular Groshong catheter is associated with fewer complications than a subclavian Argyle catheter. *European Surgical Research*; 40: 197–202.

Jaffer Y, Selby NM, Taal MW, Fluck RJ & McIntyre CW. (2008). A meta-analysis of haemodialysis catheter locking solutions in the prevention of catheter-related infection. *American Journal of Kidney Disease*; 51: 233–241.

Jain G, Allon M, Saddekni S, Barker JF & Maya ID. (2009). Does heparin coating improve patency or reduce infection of tunnelled dialysis catheters? *Clinical Journal of the American Society of Nephrology*; 4: 1787-90.

James MT, Conley J, Tonelli M, Manns BJ, MacRae J & Hemmelgarn BR. (2008). Meta-analysis: antibiotics for prophylaxis against haemodialysis catheter-related infections. Alberta Kidney Disease Network. *Annals of Internal Medicine*; 148(8): 596-605.

Johnson DW, MacGinley R, Kay TD, Hawley CM, Campbell SB, Isbel NM & Hollett P. (2002). A randomised controlled trial of topical exit-site mupirocin application in patients with tunnelled cuffed haemodialysis catheters. *Nephrology Dialysis Transplantation*; 17: 1802-1807.

Johnson DW, Van Eps C, Mudge DW, Wiggins KJ, Armstrong K & Hawley CM. (2005). Randomized, controlled trial of topical exit-site application of honey (Medihoney) versus mupirocin for the prevention of catheter-associated infections in haemodialysis patients. *Journal of the American Society of Nephrology*; 16: 1456–1462.

KDOQI 2006: National Kidney Foundation. (2006). Clinical practice guidelines and clinical practice for vascular access. http://www.kidney.org/professionals/kdoqi/guideline˙upHD˙PD˙VA/index.htm

Knuttinen M, Bobra S, Hardman J & Gaba R. (2009). A review of evolving dialysis catheter technologies. *Seminars in Interventional Radiology*; 26 (2): 106-114.

Labriola L, Crott R & Jadoul M. (2008). Preventing haemodialysis catheter-related bacteraemia with an antimicrobial lock solution: a meta-analysis of prospective randomized trials. *Nephrology Dialysis Transplantation*; 23: 1666–1672.

Landry DL, Braden GL, Gobeille SL & Haessler SD. (2010). Emergence of gentamicin-resistant bacteraemia in haemodialysis patients receiving gentamicin lock catheter prophylaxis. *Clinical Journal of the American Society of Nephrology*; 5 (10) : 1799-1804.

Lee D, Jung K & Choi Y. (2008). Use of maximal sterile barrier precautions and/or antimicrobial-coated catheters to reduce the risk of central venous catheter–related bloodstream infection. *Infection Control and Hospital Epidemiology*; 29(10): 947-950.

Levin A, Mason AJ, Jindal KK, Fong IW & Goldstein MB. (1991). Prevention of haemodialysis subclavian vein catheter infections by topical povidone-iodine. *Kidney International*; 40(5): 934–8.

Lobbedez T, Gardam M, Dedier H, Burdzy D, Chu M, Izatt S, Bargman JM, Jassal SV, Vas S, Brunton J & Oreopoulos DG. (2004). Routine use of mupirocin at the peritoneal catheter exit site and mupirocin resistance: still low after 7 years. *Nephrology Dialysis Transplantation*; 19(12): 3140-3143.

Ludlow V. (2010). Buttonhole cannulation in haemodialysis: improved outcomes and increased expense – is it worth it? *Canadian Association of Nephrology Nurses and Technologists Journal*; 20(1): 29-37.

Macrae JM, Loh G, Djurdjev, Shalansky S, Werb R, Levin A, Kiaii M. (2005). Short and long alteplase dwells in dysfunctional haemodialysis catheters. *Haemodialysis International*; 9: 189-95.

Maharaj AR, Zelenitsky SA & Vercaigne LM. (2008). Effect of an ethanol/trisodium citrate hemodialysis catheter locking solution on isolated of Candida albicans. *Haemodialysis International;* 12(3): 342-327.

Maki DG, Stolz SM, Wheeler S & Mermel LA. (1997). Prevention of central venous catheter-related bloodstream infection by use of an antiseptic impregnated catheter: a randomized, controlled trial. *Annals of Internal Medcine*; 127: 257-66.

Marr KA, Sexton D, Conlon PJ Corey GR, Schwab SJ & Kirkland K. (1997). Catheter-related bacteraemia and outcome of attempted catheter salvage in patients undergoing haemodialysis. *Annals of Internal Medicine*; 127: 275–280.

Maya ID, Carlton D, Estrada E & Allon M. (2007). Treatment of dialysis catheter-related Staphylococcus aureus bactaeremia with an antibiotic lock: a quality improvement report. *American Journal of Kidney Disease*; 50(2): 289-95.

McCann M & Moore ZE. (2010). Interventions for preventing infectious complications in haemodialysis patients with central venous catheters. *Cochrane Database Systematic Review*; 20(1): CD00689.

Mcgee DC & Gould MK. (2003). Preventing complications of central venous catheterisation. *New England Journal of Medicine*; 348: 1123-1133.

Mermel LA, Eells SJ, Acharya MK, Cartony JM, Dacus D, Fadem S, Gay EA, Gordon S, Lonks JR, Perl TM, McDougal LK, McGowan JE, Maxey G, Morse D & Tenover FC. (2010). Quantitative analysis and molecular fingerprinting of methicillin-resistant *Staphylococcus aureus* nasal colonization in different patient populations: a prospective, multicenter study. *Infection Control and Hospital Epidemiology;* 31: 592–597.

Metcalf SCL, Chambers ST & Pithie AD. (2004). Use of ethanol locks to prevent recurrent central line sepsis. *Journal of Infection*; 49: 20–22.

Moist LM, Trpeski L, Na Y & Lok CE. (2008). Increased haemodialysis catheter use in Canada and associated mortality risk: data from the Canadian Organ Replacement Registry 2001–2004. *Clinical Journal of the American Society of Nephrology;* 3: 1726–1732.

Mokrzycki MH, Jean-Jerome K, Rush H, Zdunek MP & Rosenberg SO. (2001). A randomized trial of minidose warfarin for the prevention of late malfunction in tunnelled, cuffed haemodialysis catheters. *Kidney International*; 59: 1935–1542.

Mokrzycki MH, Schroppel B, von Gersdorff G, Rush H, Zdunek M & Feingold R. (2000). Tunnelled cuffed catheter associated infections in haemodialysis patients seropositive for the human immunodeficiency virus. *Journal of the American Society of Nephrology*; 11: 2122–2127.

Moss AH, Vasilakis C, Holley JL, Foulks CJ, Pillai K & McDowell DE. (1990). Use of a silicone dual-lumen catheter with a Dacron cuff as a long-term vascular access for haemodialysis patients. *American Journal of Kidney Disease*; 16: 211-215.

Nagashima G, Kikuchi T, Tsuyuzaki H, Kawano R, Tanaka H, Nemoto H, Taguchi K & Ugajin K. (2006). To reduce catheter-related bloodstream infections: is the subclavian route better than the jugular route for central venous catheterization? *Journal of Infection and Chemotherapy;* 12: 363–5.

National Kidney Foundation KDOQI. (2001). Clinical practice guidelines and clinical practice for vascular access, update 2006. http://www.kidney.org/professionals/ kdoqi/guideline˙upHD˙PD˙VA/index.htm

Nesrallah GE, Cureden M, Wong JHS & Pierratos A. (2010). Staphylococcus aureus bacteraemia and buttonhole cannulation: long-term safety and efficacy of

mupirocin prophylaxis. *Clinical Journal of the American Society of Nephrology*; 5(6): 1047-53.

Nielsen J, Kolmos HJ & Espersen F. (1998). *Staphylococcus aureus* bacteraemia among patients undergoing dialysis—focus on dialysis catheter-related cases. *Nephrology Dialysis Transplantation*; 13: 139–145.

Onder AM, Chandar J, Billings A, Simon N, Gonzalez J, Francoeur D, Abitbol C & Zilleruelo G. (2009). Prophylaxis of catheter-related bacteremia using tissue plasminogen activator-tobramycin locks. *Pediatric Nephrology*; 24(11): 2233-43.

Pastan S, Soucie JM & McClellan WM. (2002). Vascular access and increased risk of death among haemodialysis patients. *Kidney International*; 62(2): 620–6.

Pennington CR & Pithie AD. (1987). Ethanol lock in the management of catheter occlusion. *Journal of Parenteral Nutrition*; 11: 507–5083.

Pisoni RL, Young EW, Dykstra DM, Greenwood RN, Hecking E, Gillespie B, Wolfe RA, Goodkin DA & Held PJ. (2002). Vascular access use in Europe and the United States: Results from the DOPPS. *Kidney International*; 61(1): 305–16.

Polkinghorne KR, McDonald SP, Atkins RC & Kerr PG. (2004). Vascular access and all cause mortality: a propensity score analysis. *Journal of the American Society of Nephrology*; 15(2): 477–86.

Power A, Duncan N, Singh SK, Brown W, Dalby E, Edwards C, Lynch K, Prout V, Cairns T, Griffith M, McLean A, Palmer A & Taube D. (2009). Sodium citrate versus heparin catheter locks for cuffed central venous catheters: a single center randomised control trial of sodium citrate versus heparin line locks for cuffed central venous catheters. *American Journal of Kidney Disease*; 53(6): 1034-1041.

Power A, Singh SK, Ashby D, Cairns T, Taube D & Duncan N. (2011). Long-term Tesio catheter access for haemodialysis can deliver high dialysis adequacy with low complication rates. *Journal of Vascular and Interventional Radiology;* 22(5): 631-637

Pronovost PJ, Holzmueller CG, Clattenburg L, Berenholtz S, Martinez EA, Paz JR& Needham DM. (2006). Team care: beyond open and closed intensive care units. *Current Opinion in Critical Care;* 12(6): 604-8.

Pronovost PJ, Goeschel CA, Colantuoni E, Watson S, Lubomski LH, Berenholtz SM, Thompson DA, Sinopoli DJ, Cosgrove S, Sexton JB, Marsteller JA, Hyzy RC, Welsh R, Posa P, Schumacher K & Needham D. (2010). Sustaining reductions in catheter related bloodstream infections in Michigan intensive care units: observational study. *British Medical Journal*; 4;340: 309-315

Raad I, Darouiche R, Dupuis J, Abi-Said D, Gabrielli A, Hachem R, Wall M, Harris R, Jones J, Buzaid A, Robertson C, Shenaq S, Curling P, Burke T & Ericsson C. (1997). Central venous catheters coated with minocycline and rifampin for the prevention of catheter-related colonization and bloodstream infections: a randomized, double-blind trial. *Annals of Internal Medicine*; 127: 267-74.

Rabindranath KS, Bansal T, Adams J, Das R, Shail R, MacLeod AM, Moore C & Besarab A. (2009). Systematic review of antimicrobials for the prevention of haemodialysis catheter-related infections. *Nephrology Dialysis Transplantation*; 24(12): 3763-74.

Ramos ER, Reitzel R, Jiang Y, Hachem RY, Chaftari AM, Chemaly RF, Hackett B, Pravinkumar SE, Nates J, Tarrand JJ & Raad II. (2010). Clinical effectiveness and risk of emerging resistance associated with prolonged use of antibiotic-impregnated catheters: More than 0.5 million catheter days and 7 years of clinical experience. *Critical Care Medicine*; 39 (2): 245 -251.

Regamey C, Schaberg D & Kirby WM. (1972). Inhibitory effect of heparin on gentamicin concentrations in blood. *Antimicrobial Agents and Chemotherapy*; 1: 329–332.

Ruesch S, Walder B & Tramer MR. (2002). Complications of central venous catheters: internal jugular versus subclavian access—a systematic review. *Critical Care Medicine*; 30: 454–60.

Ryan JM, Ryan BM & Smith TP. (2004). Antibiotic prophylaxis in interventional radiology. *Journal of Vascular and Interventional Radiology*; 15(6): 547-56.

Saad TF. (1999). Bacteraemia associated with tunnelled, cuffed haemodialysis catheters. *American Journal of Kidney Disease*; 34: 1114–1124.

Saxena AK, Panhotra BR, Uzzaman W, & Venkateshappa CK. (2002). The role of the *Staphylococcus aureus* nasal carriage and type of vascular access in the outcome of high-risk patients on haemodialysis. *Journal of Vascular Access*; 3(2): 74-9

Sedlacek M, Gemery JM, Cheung AL, Bayer AS & Remillard BD. (2007). Aspirin treatment is associated with a significantly decreased risk of *staphylococcus aureus* bactaeremia in haemodialysis patients with tunnelled catheters. *American Journal of Kidney Diseases*; 49: 401-408.

Shanks RM, Sargent L, Martinez RM, Graber M & O'Toole G. (2006). Catheter lock solutions influence staphylococcal biofilm formation on abiotic surfaces. *Nephrology Dialysis Transplantation*; 21: 2247–2255.

Silva GD, Silva RA, Niccolino AM, Pavanetti LC, Alasmar VL, Guzzardi R, Zanolli MB, Guilhen JC & Araujo ID. (2010). Initial experience with the buttonhole technique in a Brazilian haemodialysis center. *Journal of Brasilian Nefrology*; 32(3): 257-62.

Solomon LR, Cheesbrough JS, Ebah L & Al-Sayed T. (2010) . A randomized double-blind controlled trial of taurolidine-citrate catheter locks for the prevention of bacteraemia in patients treated with haemodialysis. *American Journal of Kidney Diseases*; 55 (6): 1060-1068.

Taal MW, Fluck RJ & McIntyre CW. (2006). Preventing catheter related infections in haemodialysis patients. *Current Opinion in Nephrology and Hypertension*; 15(6): 599-602.

Takla TA, Zelenitsky SA & Vercaigne LM. (2007). Effect of ethanol/trisodium lock on microorganisms causing haemodialysis related catheter infections. *Journal of Vascular Access*; 8(4): 262-7.

Taylor C, Cahill J, Gerrish M, & Little J. (2008). A new haemodialysis catheter-locking agent reduces infections in haemodialysis patients. *Journal of Renal Care*; 34(3): 116-120.

The European Renal Association - European Dialysis and Transplant Association. European best practice guidelines for haemodialysis (Part 1) ERA-EDTA. (2002). *Nephrology Dialysis Transplantation*; 17: (Suppl 7):1–111.

Timsit JF, Schwebel C, Bouadma L & Geffroy A. (2009). Chlorhexidine-impregnated sponges and less frequent dressing changes for prevention of catheter-related infections in critically ill adults: a randomized controlled trial. *Journal of the American Medical Association*; 25: 301(12): 1231-41.

Tordoir J, Canaud B, Haage P, Konner K, Basci A, Fouque D, Kooman J, Martin-Malo A, Pedrini L, Pizzarelli F, Tattersall J, Vennegoor M, Wanner C, ter Wee P & Vanholder R. (2007). EBPG on Vascular Access. *Nephrology Dialysis Transplantation*; 22 [Suppl 2]: ii88–ii117.

Torres-Viera C, Thauvin-Eliopoulos C, Souli M, DeGirolami P, Farris MG, Wennersten CB, Sofia RD & Eliopoulos GM. (2000). Activities of taurolidine in vitro and in

experimental enterococcal endocarditis. *Antimicrobial Agents and Chemotherapy*; 44(6): 1720-1724.

Trerotola SO, Patel AA, Shlansky-Goldberg RD, Solomon JA, Mondschein JI, Stavropoulos SW, Soulen MC, Itkin M & Chittams J. (2010). Short-term infection in cuffed versus noncuffed small bore central catheters: a randomized trial. *Journal of Vascular and Interventional Radiology*; 21: 203–11.

Tumlin J, Goldman J, Spiegel DM, Roer D, Ntoso KA, Blaney M, Jacobs J, Gillespie BS & Begelman SM. (2010). A phase III, randomised, double-blind placebo-controlled study of tenecteplase for improvement of haemodialysis catheter function: TROPICS 3. *Clinical Journal of the American Society of Nephrology*; 5: 631-6.

United States CDC (Centers for Disease Control and Prevention). Guidelines for the prevention of intravascular catheter-related infections (2002). http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5110a1.htm : 1–26.

Van Eps CL, Jones M, Ng T, Johnson DW, Campbell SB, Isbel NM, Mudge DW, Beller E & Hawley CM. (2010). The impact of extended-hours home haemodialysis and buttonhole cannulation technique on hospitalization rates for septic events related to dialysis access. *Haemodialysis International*; 14(4): 451-63.

Van Loon MM, Goovaerts T, Kessels AGH, van der Sande FM & Tordoir JHM. (2010). Buttonhole needling of haemodialysis arteriovenous fistulae results in less complications and interventions compared to the rope-ladder technique. *Nephrology Dialysis Transplantation*; 25: 225-30.

Vercaigne LM, Takla TA & Raghavan J. (2010). Long-term effect of an ethanol/sodium citrate solution on the mechanical properties of haemodialysis catheters. *Journal of Vascular Access*; 11(1): 12-6.

Weijmer MC, van den Dorpel MA, Van de Ven PJG, ter Wee P, van Geelen J, Groeneveld J, van Jaarsveld BC, Koopmans M, le Poole C, Schrander A, Sieger C & Stas KJ. (2005). Randomized, clinical trial comparison of trisodium citrate 30% and heparin as catheter-locking solution in haemodialysis patients. *Journal of the American Society of Nephrology*; 16: 2769-2777.

Xue J, Dahl D, Ebben J & Collins AJ. (2003). The association of initial haemodialysis access type with mortality outcomes in elderly Medicare ESRD patients. *American Journal of Kidney Diseases*; 42(5): 1013-1019.

Yahav D, Rozen-Zvi B, Gafter-Gvili A, Leibovici L, Gafter U & Paul M. (2008). Antimicrobial lock solutions for the prevention of infections associated with intravascular catheters in patients undergoing haemodialysis: systematic review and meta-analysis of randomized, controlled trials. *Clinical Infectious Diseases*; 47: 83–93.

Yoo S, Ha M, Chio D & Pai H. (2001). Effectiveness of surveillance of central catheter-related bloodstream infection in an ICU in Korea. *Infection Control and Hospital Epidemiology*; 22: 433–436.

Yu VL, Goetz A & Wagener M. (1986). *Staphylococcus aureus* carriage and infection in patients on haemodialysis. Efficacy of antibiotic prophylaxis. *New England Journal of Medicine;* 315: 91–96.
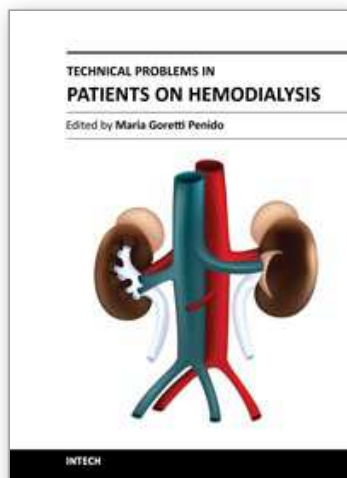
Technical Problems in Patients on Hemodialysis

Edited by Prof. Maria Goretti Penido

This book provides an overview of technical aspects in treatment of hemodialysis patients. Authors have contributed their most interesting findings in dealing with hemodialysis from the aspect of the tools and techniques used.Each chapter has been thoroughly revised and updated so the readers are acquainted with the latest data and observations in the area, where several aspects are to be considered. The book is comprehensive and not limited to a partial discussion of hemodialysis. To accomplish this we are pleased to have been able to summarize state of the art knowledge in each chapter of the book.

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