

Pin and needle tract infection: the prophylactic role of silver

Silver is widely used in wound dressings and medical devices to control pathogenic infections which are recognised as causes of impaired healing, functional defects in orthopaedic fixation pins and patient distress. This review discusses new approaches and advances in silver technology in controlling infections associated with wound sutures, insertion points and in-dwelling catheters, gastrostomy tubes and orthopaedic fixation pins. The author discusses silver-coated and silver-containing sutures and considers efficacy, safety in use and the possibility of silver resistance.

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KEY WORDS

Silver technology

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Skin wounds vary greatly in their causation, severity, pathological characteristics and capacity to heal (Grey and Harding, 1998; Dow et al, 1999; Bowler, 2003). All wounds breaching the epidermal barrier function are prone to infection from opportunist pathogens from a patient's own body flora and from the nosocomial environment. Current views on wound repair and tissue regeneration focus increasingly upon appropriate wound bed preparation with elimination of pathogenic infections and establishment of an appropriate bacterial balance (Enoch and Harding, 2003; Schultz et al, 2003). Considerable emphasis has been placed upon the prophylactic value of silver; silver sulphadiazine and wound

dressings that release silver ions in the presence of moisture and wound exudates (Lansdown, 2002a,b; 2005).

Silver has a proven efficacy against a wide spectrum of bacteria, fungi and yeasts and various dressings, which have been tailored to treat specific wound types, provide great advantages in the management of heavily exuding ulcers, malodorous conditions and patient discomfort (Ovington, 2001; White, 2001). Whereas the literature is replete with highly relevant information on the value of silver in treating chronic wounds and burns, less attention has been placed on its value in controlling infections associated with wound suture insertion and sites of percutaneous penetration of medical devices including in-dwelling catheters, external fixation pins used in orthopaedic surgery and acupuncture needles. Many infections commonly encountered in wound care may colonise penetration sites and lead to biofilm formation (Donlon, 2002; Dunne, 2002). Biofilms are a recurrent problem in the use of medical devices, especially catheters where they can lead to functional impairment and severe discomfort for the patient (Elliott, 1999; Saint et al, 2002).

Silver-coated external fixation pins, percutaneous enterostomal gastrostomy (PEG) devices, catheters

for intravascular, intraperitoneal or suprapubic insertion and other devices for surgical intervention are not currently available in the UK at the present time, but are subject to research in the USA and in other parts of Europe. A survey of the literature reveals three main lines of research into the control of infections associated with surgical incisions, medical devices and other surgical interventions:

- ▶▶ The use of metallic silver in surgical knives, sutures and orthopaedic pins
- ▶▶ Topical application of silver nitrate, silver sulphadiazine or silver ion release dressings to wound sites
- ▶▶ Silver coating of materials used in the manufacture of medical devices.

In each case, the ionised silver released is highly reactive and readily binds tissue debris, albumins, macro-globulins and proteins in wound exudates and tissue secretions. It interacts with receptors on cell membranes and is metabolised and possibly mobilised as a complex with metallothionein or other metal binding proteins (Lansdown, 2002a), with a small proportion reaching the systemic circulation. Unbound silver ion is available for antimicrobial action either through liberation into the wound bed (Acticoat[®], Smith & Nephew, Hull; Urgotul[®], Urgo, Chenôve) or within the dressing as in Aquacel[®] Ag (ConvaTec, Ickenham) or Contreet[®] Foam (Coloplast, Peterborough).

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Silver ions released from topical applications can be expected to control mainly superficial infections whereas silver or silver-coated sutures, catheters, fixation pins, screws and surgical needles, should release biologically active ions through the entire depth of the incision or device tract, to control deeper infections. Ideally, silver used in the construction of medical devices will release silver ions for the entire duration of use. This article will discuss clinical and experimental evidence for the antimicrobial efficacy of silver and silver-coated devices in controlling percutaneous infections. Since 'implantation' of silver in the body in medical devices is liable to lead to higher blood silver levels (argyraemias), emphasis is placed upon safety in use of silver or silver-coated medical devices.

Silver in controlling superficial infections at device insertion sites

Historically, silver has made many contributions in controlling postoperative infection in surgical wounds. Silver surgical knives appear in historical collections and records exist of silver needles, silver thread and silver prostheses in early medicine. Ambrose Paré (1517–90) used silver clips in facial reconstruction, and William Halstead (1895) employed silver wire sutures in surgery for hernias. He recorded that silver foil provided an effective barrier against postoperative infections. Other early studies concluded that since silver nitrate readily formed precipitates with albumin and sodium chloride, its local action as an astringent and antibiotic could be readily controlled (Lubinski, 1914). Lubinski (1914) considered erroneously that the antimicrobial action of silver would extend 'quite deeply' into a wound on account of its ability to bind albumins and inorganic anions in the wound site. We now know that the reverse is true, and that silver complexes forming in the wound bed inhibit penetration (Lansdown et al, 1997; Lansdown and Williams, 2004). Although metallic silver releases less than 1 ppm Ag⁺, this is probably sufficient to control infections in the acute phase. Nanocrystalline silver preparations releasing appreciably more ions can be expected to provide more

efficacious action in heavily infected conditions (Burrell, 2003; 2004).

Inorganic salts of silver, especially nitrate, are astringent and irritant but show antiseptic effects. Lowbury (1972) used 0.5% silver nitrate to reduce *Pseudomonas aeruginosa* infection in patients with burn wounds from about 70% to 3%. Silver nitrate is still used to control life-threatening infections including *P. aeruginosa* and *Staphylococcus aureus* in burn wounds, but its irritancy and astringency would preclude its routine use in disinfecting superficial wounds associated with indwelling catheters or other medical devices. The caustic properties of silver nitrate are now licensed by the Medicines Control Agency (UK) as toughened silver nitrate for removal of warts, verrucae and unsightly granulations (Avoca®, Bray Healthcare, Faringdon). It recommends extreme caution when applying the preparation. The manufacturers claim that silver nitrate fused with potassium nitrate in the form of a caustic pencil is safer and less painful for patients than more corrosive or systemically administered therapies. It has been used effectively in the author's clinic at Charing Cross Hospital to treat a local infection associated with a protruding bone fragment (Figure 1). (The silver deposits appear as blackish discolourations.)

While it may be common practice in many clinics to treat infections at sites of insertion of intravascular or intraperitoneal catheters, enterostomal

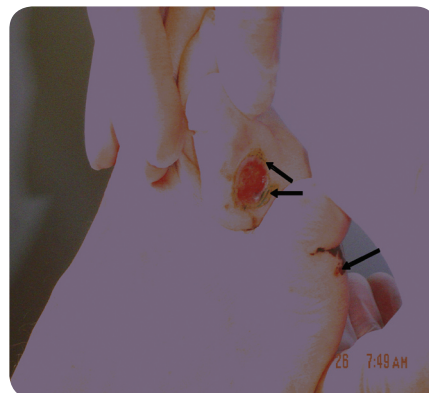


Figure 1. Silver nitrate used to treat protruding bone fragment.

gastrostomy devices and suprapubic drainage with sustained silver release dressings, tracheostomy and so on, few cases of infections have actually been reported. Leak (2002) drew attention to infections associated with profound granulation and high levels of exudate at percutaneous endoscopic gastrostomy (PEG) sites and how they can be effectively treated with sustained silver-release dressings such as Actisorb Silver 220 (Johnson & Johnson Wound Management, Ascot). In Leak's opinion, the inherent risks of superinfection, sensitisation and emergence of antibiotic-resistant strains precluded the routine use of antibiotics in the treatment of colonised or infected wounds. On the other hand, sustained silver ion release dressings are convenient to apply, safe and effective in controlling bacterial balances, malodours and resulting inflammatory changes in surrounding skin (Lansdown and Williams, 2004; Lansdown et al, 2005). In a pilot study, Leak (2002) successfully employed Actisorb Silver 220 to treat PEG site infections where prolonged pressures and excessive exudates had led to some maceration. The practice is now more widely adopted in the Doncaster Royal Infirmary where the pilot study was carried out.

As an alternative to treating PEG or catheter exit sites with silver dressings earlier studies evaluated the use of silver cuffs located around the devices at the points of entry or subcutaneously (Figure 2). Große-Siestrup et al (1992) conducted a clinical study of 20 patients implanted with peritoneal dialysis catheters fitted with a silver ring which was gently eased into exit sites allowing release of silver ions into the wound

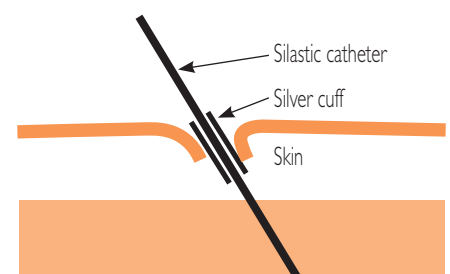


Figure 2. Silver Cuff Technique to prevent Catheter Exit Site Infections.

margin. The technique was effective in eliminating *S. aureus*, *S. epidermidis* and *Escherichia coli* infections in eight patients while maintaining germ-free status in 11 of the remaining 12. Groeger et al (1993) conducted a similar prospective evaluation using silver-impregnated subcutaneous cuffs to prevent 'tunnelled' infections associated with chronic venous access catheters in 92 patients with cancer. Results were less impressive, with infections being diagnosed at insertion sites in seven patients (12 in the control group) with no significant difference in infection rates during the lifetime of the catheters. However, the overall incidence of catheter tunnel infections in this cohort of patients was insufficient to allow a valid statistical evaluation.

Bhattacharyya and Bradley (2006) provided an example of how a silver-release dressing might be used in the topical management of infections due to medical devices, such as orthopaedic K-wires. These wires, used in the external fixation of orthopaedic fractures, commonly protrude from the skin with insertion points and tracts providing easy access for opportunist pathogens to vulnerable tissues of the dermis and deeper. Infection rates associated with external fixation devices of 21–85% are a cause for severe discomfort to patients as well as instability of pins and impairment of their orthopaedic function. Bhattacharyya and Bradley (2006) treated pin tract infections in 11 older patients (mean age=66.8 years) with Acticoat-7 dressings (Smith and Nephew, Hull) and monitored their progress over 42 days postoperatively. Although overt signs of infections at the external orifice of external fixation pins were controlled and wound sites healed well following exposure to Acticoat-7 dressing, this treatment was not superior to that achieved with oral antibiotic therapy. Although details of the nature or severity of the infections were not included, the authors maintained that a topical dressing such as Acticoat-7 is preferred to oral antibiotics in older patients, for reasons of safety and ease of management.

Silver in surgical procedures

Infections encountered at needle and incision sites are potentially the most frequent problems arising through perforation of the epidermal barrier layer (Darouiche, 1999). The presence of xenobiotic materials such as suture materials, needles, prosthetic devices, external fixation pins and catheters, greatly enhances the risk of infection; and the majority of wound infections initiate along and in the vicinity of suture lines (Sugarman and Young, 1984; Tsai et al, 1987). Most can be avoided through good hygienic clinical practice, use of sterile equipment and appropriate postoperative care. Whereas it might have been common practice a few years ago to use silver surgical knives, silver-coated or silver alloy needles, and silver wire sutures to control postoperative infections, it is rare practice these days, except possibly in ophthalmic surgery (Kloti, 1974; Nasr et al, 1983; March et al, 1987) and in acupuncture (Tanita et al, 1985; Yi-Kai et al, 2000).

Acupuncture needles made of silver or gold are used as part of Hari therapy for headache, fatigue, back pain etc in oriental medicine (Tanita et al, 1985). Needles consisting of silver or gold are implanted intracutaneously and possibly left within the skin for several days. Infection does not seem to be a reported problem of needle insertion sites in acupuncture but excessive release of silver ion is an occasional cause of blue macules of argyria at insertion points and elsewhere in the body (Suzuki et al, 1993; Takeishi et al, 2002; Kakurai et al, 2003). Chrysiasis due to accumulation of dark complexes of gold are occasional complications. Neither condition is of toxicological significance but the discolourations are cosmetically undesirable.

Silver sutures

Metallic sutures have been used by surgeons since the times of the early Greeks when Galen (130–200 AD) is reputed to have used ligatures of gold wire (Rucker, 1950). Over the centuries, surgeons have employed lead, stainless steel, silver wire and

a variety of non-metallic suture materials coated with a silver ion release compound (such as silver zeolite or silver oxide) (Bright et al, 2002; Blaker et al, 2004). The first recorded use of silver sutures derives from gynaecological surgery, when J Marion Sims (1849) sought to improve on his ability to close indolent vaginal fistulae. In his 30th operation, he successfully used silver wire to close a major fistula and reported that not only had the wound healed well but that surrounding tissues were not inflamed or subject to overt adverse reactions. In 1987 Bashir noted that daily twisting of silver wire advances re-epithelialisation in surgical repair.

Darouiche (1999) examined the antimicrobial efficacy of silver-treated medical sutures used in surgery and drew attention to the lack of success in early studies where materials such as silk, polyethylene terephthalate (Dacron), and catgut, were immersed in 5% or 50% silver nitrate for 24 hours. They failed to inhibit *S. aureus* infection. Later studies found that using a silver-zinc allantoinate complex was more successful in controlling staphylococcal infections, possibly on account of the more sustained release of bactericidal levels of silver ions, and the reduced binding of silver to the suture materials (Gravens et al, 1973).

In one form or another, silver molecules have been incorporated into the surfaces of a large number of medical devices with a view to limiting infections. It is unfortunate that as new technology comes to hand with new advances in nanotechnology, few have been fully evaluated and their real clinical value appreciated. Cowan et al (2003) refer to the value of silver zeolite coating for stainless steel and its capacity to reduce colony formation of *E. coli*, *S. aureus* and other bacteria in vitro, but emphasise that the stability of the coating and duration of its antimicrobial action must be clarified before the technology can be developed for clinical use. Whereas significant reductions in 'colony-forming units' were reported with five

bacterial strains commonly seen in skin wounds within four hours of exposure, this effect diminished markedly when the coatings had been applied by a 'wet process' and scrubbed between uses. Power-coated surfaces cleansed with a towel offered a higher degree of antibacterial efficiency.

A quite different approach to antimicrobial sutures derives from research in materials science at Imperial College, London. Following successes achieved in orthopaedic surgery with the biodegradable composite Bioglass® (Novabone, Florida) (Figure 3) (Wang et al, 1998; Bellantone et al, 2000; 2002), Blaker et al (2004; 2005) engineered a new bioactive suture with antimicrobial properties. Bioglass® is a family of bioactive glasses that elicit specific physiological responses in hard and soft tissues through release of calcium, silicon and phosphate. By incorporating silver oxide in this composite Blaker et al have developed an antimicrobial molecule. Using a 'slurry dipping' technique, commercially available resorbable sutures — polyglactin 910 (Vicryl or the non-resorbable material Mersilk, both from Ethicon, Livingston), were coated with Bioglass® granules to provide new suture material for surgery (Figure 4). Physico-chemical analyses substantiated that this bioactive glass coating did not significantly influence the tensile strength or thermal properties of the suture materials and released sufficient silver in a sustained fashion to control *S. epidermidis* isolates in vitro (Pratten et al, 2004). The new suture was effective in limiting bacterial attachment and is predicted to have many applications in wound healing and general surgery. Experimental studies indicate that the silver Bioglass® complex degrades completely in the wound bed to release silver; silicon and calcium ions, each with a defined role in tissue repair (Lansdown et al, 1997; Carlisle, 1982; Lansdown, 2002c). Preliminary evaluation of the suture in experimental wounds demonstrated the central role of dermal macrophages in the catabolism of the Bioglass® complex and in the metabolism of silver (Figure 5), calcium and silicon in

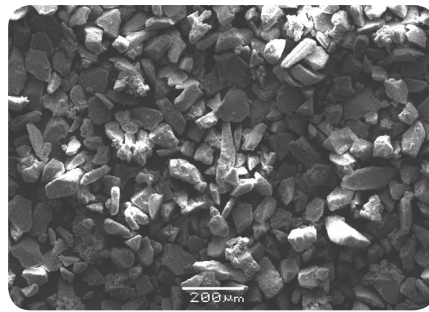


Figure 3. Bioglass® Granules observed by Scanning Electron Microscopy.

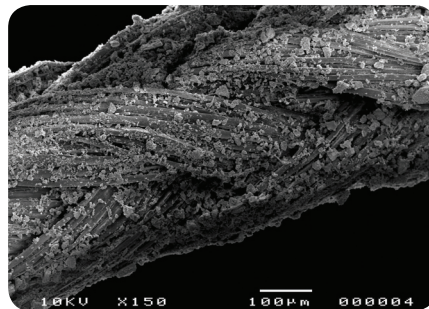


Figure 4. Mersilk® Fibre doped with silver oxide as an antimicrobial suture.

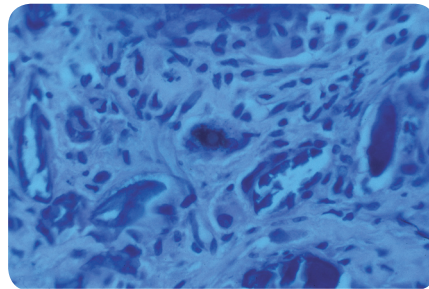


Figure 5. Dermal macrophage in a rat wound containing cytoplasmic granules of silver (x40 objective).

the wound bed as a prerequisite for epidermal regeneration and tissue repair (Lansdown et al, 2003). The product is without detectable adverse effects and wounds healed normally during the study.

Although electrical currents have been used to accentuate silver ion release from silver wire or foil for many years (Spadaro et al, 1974; Becker, 1986), its application in the use of a braided nylon suture impregnated with a silver compound is of interest (Chu et al, 1987; Tsai et al, 1987). In these related studies a silver-containing nylon suture (Nurulon [Ethicon, Livingston]) was connected to a direct electric current and shown to inhibit

seven strains of wound bacteria in tissue culture. The responses were mixed, whereas *P. aeruginosa* was most sensitive to silver released at anodes, *Proteus mirabilis*, which presents major problems by creeping along encrusting medical devices, was least sensitive.

External fixation pins

Clayton Parkhill (1897) was possibly the first surgeon to use silver-coated devices to fix bone fractures, his steel clamp being heavily coated in silver to provide antiseptic action. Parkhill attempted to create an 'unfavourable environment' on the surface of the fixation devices to limit bacterial adhesion and this has also been attempted more recently (Shintani, 2004). This concept has been developed widely in the design of orthopaedic pins and screws which are commonly colonised by bacterial flora, notably *S. aureus* and *S. epidermidis* (Bosetti et al, 2002). Biofilm formation is an additional problem in orthopaedic medicine and fixation devices are subject to infections such as *P. mirabilis* which adhere to exposed surfaces and migrate along solid surfaces to aggregate and form mineralised concretions or calyces (Morris et al, 1997). This results in instability of the devices and can be a cause of severe patient discomfort. Devices including xenobiotic implants and fixation devices are not inert but interact with their surrounding environment (Wassall et al, 1997; Darouiche, 1999). Bacterial colonisation may not be immediately obvious but can be expected to increase proportionately with the period for which the fixation pins are in place which was shown by Respet et al (1987) in canine experimentation.

Pin tract infections may occur in 2–30% of all implants (Green, 1983; Massè et al, 2000). Biofilms are made up of mixed populations of organisms commonly seen in skin wounds; they mutate readily and become resistant to many antibiotics (including silver) with colonies providing reservoirs from which organisms contaminate surrounding tissues as well as systemically (Sheehan et al, 2004). Resistance plasmids between different

bacterial strains are readily exchanged by conjugation. Problems associated with biofilm formation in the use of orthopaedic devices, catheters for intravascular, intraperitoneal or suprapubic insertion, orthopaedic prostheses and bone cements and other medical devices are fully discussed elsewhere (Donlan, 2002; Dunne, 2002). Whereas early studies indicated that silver coating was an efficacious means of controlling bacterial adhesion and colony formation associated with pins and devices for fixation of bone fractures, this has not been substantiated in experimental or clinical studies (Darouiche, 1999).

The hypothesis that silver coating will decrease bacterial colonisation and pin tract infections has led to a range of technologies and experimental studies in rabbits and sheep. In early studies, Colmano et al (1979; 1980) implanted intramedullary silver-electroplated pins in rabbit femurs and applied a direct electric current. Stainless steel pins coated with 100 monomolecular layers of silver stearate resulted in a 69% reduction of *S. aureus* within one hour. These observations compared favourably with later work in which stainless steel pins were coated with silver (2.5%) and zinc (14%) zeolite (Bright et al, 2002) without use of an electric current (Cowan et al 2003).

The SPI-Argent technology (Spire Biomedical, Bedford, Mass) has been subject to more comprehensive investigation (Collinge et al, 1994; Wassall et al, 1997; Massè et al, 2000). Silver coating of orthopaedic fixation pins and screws was achieved by exposing stainless steel to an ion-beam assisted deposition of silver granules (50–150nm diameter) from a vapour phase. The technology enabled deposition of a homogenous coating of silver on the surface of stainless steel. Distribution patterns have been monitored using scanning electron-microscopy and energy dispersive X-ray analysis (EDAX) (Wassall et al, 1997). Preliminary studies showed that while the silver

coating was effective in reducing the incidence of *E. coli*, *P. aeruginosa* and *S. aureus* on orthopaedic pins in vitro, it actually enhanced the adhesion of *Staphylococcus haemolyticus* (Wassall et al, 1997). Further, when 36 silver-coated and 12 uncoated stainless steel pins were implanted into the iliac crest of six sheep and inoculated with *S. aureus*, 84% of the uncoated pins were infected while only 62% of the silver-coated pins were infected as shown by electron microscopy (Collinge et al, 1994). This difference is not statistically significant but silver-coated pins were loose less frequently than uncoated pins and pin motion was closely correlated with infection. Not unexpectedly, when silver-coated fixation pins were pre-conditioned by exposure to human serum, bacterial adhesion was in most cases significantly greater than in unconditioned pins. Albumins and macroglobulins in the serum reduced the efficacy of the silver by binding free ions (Wassall et al, 1997). Similarly unconvincing observations were made in an experimental study where silver-coated K-wires were inserted into rabbit femurs to mimic conditions of human orthopaedic surgery (Sheehan et al, 2004). This study further confirmed the limited capacity of silver to control biofilm formation, at least with *S. aureus* and *S. epidermidis*.

Clinical evaluation of SPI-Argent treated external fixation pins/screws in the management of limb fractures in 24 male patients demonstrated a reduction in pin tract infections, but the observations were not significantly different from those seen in patients treated with commercially available stainless steel devices (Massè et al, 2000). *S. aureus* was most frequently cultured from screw tips. Ethical considerations and a lack of statistically significant observations resulted in a discontinuation of the work. No adverse effects were seen in or near implantation sites, including overt signs of infection.

Colloidal silver has been used to coat external fixation pins in an effort to remove risks of pin tract infections

(Meyer et al, 2004). In a sheep model, stainless steel, titanium, colloidal silver-coated and stainless steel pins coated in a polyurethane-silver sleeve were evaluated. Although there was a trend towards lower infection rates for *S. aureus* infection for the silver-treated pins, the effect was not significantly different from other pin types. Although colloidal silver exhibited no appreciable influence on pin tract infections, it was reported to show improved results regarding osteolysis caused by *S. aureus* infection.

Coating orthopaedic implants with an antimicrobial layer of titanium/silver (2µm thick) via a physical vapour deposition process in an inert atmosphere of argon was evaluated recently for antibacterial efficacy (Ewald et al, 2006). Although titanium has no recognised antibacterial effect, this coating released 0.5 to 2.3ppb silver when immersed in saline and exhibited significant antimicrobial potency against *S. aureus* and *Klebsiella sp.* As in previous studies (Bosetti et al, 2002), the silver-coating technology was without adverse effects on osteoblasts and epithelial cells in culture. Clinical evaluation is awaited.

Safety in use

Use of silver metal, silver impregnation or silver coating in medical devices for implantation, pin tracts or exit sites in the body wall has not generally given rise to concern about toxicology. Allergy and delayed hypersensitivity to silver have not been recorded and confirmed reactions to silver in regions local to implants or elsewhere in the body are rare. Limited subjective observations suggest that silver acts as an anti-inflammatory agent. Wound sites have been reported to heal well following removal of silver-coated devices with no obvious sequelae (Massè et al, 2000). Darouiche (1999) did add the caveat that it is prudent to ensure that, while constructing silver-coated medical prostheses or other devices, silver is incorporated onto the surfaces at concentrations that are adequate for the reduction of bacterial adhesion but not high enough to evoke systemic toxicity.

Release of silver ions from the various devices discussed has been quantified using energy dispersive X-ray spectrometry but rarely have silver levels in the blood been measured. Massè et al (2000) in their clinical evaluation of fixation pins coated by the SPI-Argent method, reported a rise in blood silver from 0.2µg/l to a medial level of 2.79µg/l after seven days and 3.2µg/l after two months. Although this rise is statistically significant, it is substantially below threshold limit values set by the Food and Drug Administration of the USA and the 14µg/l reported as an acceptable non-toxic value for precious metals derived from a literature search (Perrelli and Piolatto, 1992).

Discussion

Silver is a well recognised antimicrobial agent with a broad spectrum of action against opportunist pathogens infecting wound sites. While numerous clinical trials have demonstrated the ability of the various sustained silver ion release dressings to control microbial flora in acute and chronic wounds, a limited experience, discussed above, points to their capacity to limit infections at sites of insertion (and exit) of medical devices including orthopaedic fixation pins and gastrostomy devices which protrude from the skin for several days or weeks.

Experience has shown that although silver, silver nitrate and dressings that release silver ion do control wound flora and aid, and thereby advance wound bed preparation, they rarely lead to a germ-free wound site. Also there is often poor agreement between in vitro trials that test for antimicrobial action against named pathogens (usually bacteria) and clinical experience. This situation is true both in the case of dressings designed for chronic skin wounds and ulcers, and in the preparation of medical devices including catheters, intraperitoneal drainage devices, wound sutures and external fixation pins/screws treated with silver metal or other ionisable silver compound.

Reduced antimicrobial action of silver-containing dressings or silvered medical devices is attributable to three main causes:

- ▶▶ Silver-resistant organisms (including biofilm formation)
- ▶▶ Insufficient 'available' silver ion in the medium, wound bed, pin or needle tract to exert a lethal action on sensitive strains
- ▶▶ Epigenic mechanisms.

Although skin wounds, orthopaedic fixation pin implantation sites, PEG drainage and even suturing may provide a sufficiently stressful environment to select for antibiotic resistance (Gupta et al 1999), there is no tangible evidence so far to show that it actually occurs. Silver-resistant bacteria have been identified in patients with burn wounds, water effluents and photographic sludges, but available information indicates that it is a rare event (Russell and Hugo, 1994; Percival et al, 2005). There is no substantive evidence to show that prolonged exposure to silver in any clinical situation predisposes to silver resistance.

Preliminary studies in the author's laboratory have shown that all but one bacterium isolated from chronic ulcer patients is sensitive to silver (1.0mM AgNO₃) in plate culture; a strain of *Enterobacter cloacae* was found to grow in the presence of 1.0mM AgNO₃ and revealed molecular evidence of genetical resistance to silver (Lansdown et al 2004a; 2005). This suggests that the large proportion of bacteria in a wound site exposed to metallic silver, silver coatings or silver ion releasing dressings should be killed.

Burrell et al (2004) estimated that silver ion should be available at concentrations of 10–40ppm to kill most organisms and 60ppm to eliminate the most resistant strains including methicillin-resistant *S. aureus*. Although wide variations exist in the actual amount of silver released by the various wound dressings and silver-treated medical devices, it is important to recognise that the antimicrobial effect can only be measured in terms of

the amount of silver actually 'available' over and above that bound in stable complexes with inorganic anions, albumins and macroglobulins in wound exudates and secretions, and to living tissues of the host.

Nanocrystalline silver as the bioactive principle of Acticoat® (Smith & Nephew, Hull) and some antibiotic coatings for medical devices releases 70–100µg Ag⁺/ml in the presence of moisture and wound fluids, whereas metallic silver (foil, coating, wire) possibly releases less than 1µg/ml (Burrell, 2003; 2004). Data is not available for silver zeolite or colloidal silver as used in some coatings. Clearly, the relative inefficiency of the silver or silver coating in reducing bacterial adhesion and device-related infections must be attributable to the fact that in pin, needle and device tracts, silver ion binding to host tissues and exudates outweighs the amount available for antimicrobial action. Even in tissue culture, silver ion is readily bound to chloride ion, nutrients in the agar medium and electrolytes. This means that as in preliminary studies by the author, a concentration of silver nitrate of 1.0mM necessary to kill most wound bacteria in a wound is not a true reflection on the silver concentration to be obtained in a wound bed for total bactericidal action.

Epigenic (non-genetic) mechanisms of microbial resistance to silver or other metal cations are not well defined. Studies by Gupta et al (1999) have demonstrated that the action of silver on sensitive bacteria and fungi is largely attributable to a genetically-mediated uptake of lethal concentrations of ionic silver. However, they also report that halide ions in the medium can influence the expression of natural sensitivity or resistance to silver (Gupta et al, 1998). Low concentrations of silver increased the minimal inhibitory concentration between sensitive and resistant strains, high levels of halide increased the sensitivities of both strains. The extent to which this or other epigenic mechanisms contribute to reduced antimicrobial efficacy in in-dwelling medical devices is not known.

Key Points

- ▶▶ Silver is an efficacious anti-microbiological agent which ionises in the presence of moisture or wound fluids to kill genetically-sensitive organisms.
- ▶▶ Silver ions released from medical dressings and surgical devices are effective in controlling infections and improving the clinical use of orthopaedic fixation pins, catheters and devices inserted percutaneously.
- ▶▶ New technology has led to development of silver-coated or silver-containing sutures, indwelling catheters, orthopaedic fixation pins and other medical devices commonly subject to infection and biofilm formation.
- ▶▶ Silver products are generally safe for patients, but risks of silver hypersensitivity and allergy do occur. The true incidence of silver-resistant bacteria in clinical practice is not known.

Conclusions

In conclusion, silver is widely used in clinical situations where infection is expected to be a cause for patient ill health and distress. New technology and new products have led to greater understanding of the importance of balancing the release of silver ions to achieve maximal microbicidal efficacy without compromising the health of patients. Present views are that although silver-release dressings, silver coatings and other silver technologies used in patient care have achieved many successes in controlling infections and achieving the so-called bacterial balances in tissues, further research is still required to understand the true extent of

silver resistance in bacteria and the relative inactivity of silver on biofilm formation. **WUK**

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