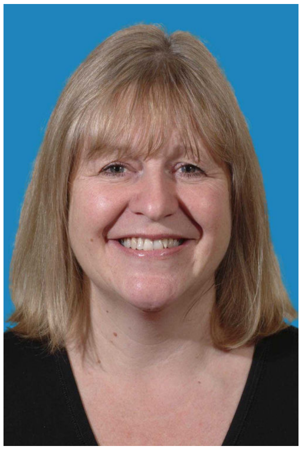
Professor Joanna Verran writes on the interactions occurring between micro-organisms and PVC-U cable containment systems.



Joanna Verran is Professor of Microbiology in the School of Biology, Chemistry and Health Science at Manchester Metropolitan University.

Her research is interdisciplinary, involving collaboration with materials scientists, polymer and dental technologists and surface engineers, and focusing on the interactions occurring between microorganisms and inert surfaces. The effect of changes in surface chemistry and topography on these interactions, and effects on hygienic status and cleanability are of particular interest. The presence of non-microbial inorganic and organic material can also affect these parameters. Applications therefore address food, water and environmental aspects, as well as the oral health of denture wearers. Professor Verran also has a keen and active interest in microbiology education.

Specifying Cable Containment Systems with Antimicrobial Properties: what you need to know.

Introduction - rationale

Trunking systems provide protection for cables and, ideally, also an aesthetic appearance, coupled with easy cleanability. Such systems and surfaces will be exposed within a wide range of environments, including hospitals and other environments where hygiene is of concern, thus any modifications that will improve cleanability and enhance hygienic status are desirable.

For cleanability, rounded edges, smooth jointing, and a colour that enables visible dirt to be easily detected are prime considerations. For hygienic status, the incorporation into the trunking system of an antimicrobial agent provides one approach.

The requirements of such technology encompass consumer and environmental safety, compliance with the European Biocidal Product Directive and so on – but also of concern is effectiveness against microorganisms under conditions of use.

Microorganisms transferred onto a surface may die (the most favourable scenario!), survive, or multiply (given appropriate conditions for growth). Viable cells therefore pose a 'biotransfer potential'. They may be transferred to a less inert substratum, such as the human skin, a wound, food etc., where multiplication and subsequent potential for damage are enabled.

Microorganisms are present in all environments and many are undesirable. In the food environment, the absence of pathogens such as *Salmonella* and *Listeria* is an obvious target but spoilage microorganisms will also affect the quality of the food and hence its value to the producer. In other environments, where large numbers of people might be present and where hygiene may not be a prime concern due to the overall good health of the population – for example schools, sports and health centres – the presence of easy to clean surfaces coupled with additional antimicrobial properties may help reduce the transfer of microorganisms such as those associated with colds and other respiratory infections or wound and skin infections, from person to person via surfaces.

Dental surgeries, and laboratories involved in the preparation of medical/surgical/dental devices provide additional environments where infection control is important. In nursing and care homes, residents are usually elderly and often not in good health. Their reduced ability to cope with illness makes them susceptible to infection thus, again, hygienic surfaces coupled with excellent cleaning and disinfection and other infection control protocols will help maintain and improve the overall health of the population.

In the hospital environment, patients are particularly susceptible to infection, thus reduction in the transfer of microorganisms directly from person to person and indirectly via inanimate objects, is a key objective. The microorganisms present may also be more resistant to antibiotics, since resistance provides an advantage in the environment where antibiotics are in regular use.

Thus, patients are at risk from pathogens (microorganisms that cause disease); opportunist pathogens (microorganisms that can cause disease given the opportunity – for example via wound infection) with the additional possibility of enhanced resistance to antibiotics. Hospital acquired infections (HAI), also called Health-care associated infections (HCAI) are the umbrella terms typically used to describe these infections.

This paper provides an overview of the use of silver technology focused towards an antimicrobial treatment for cable trunking. In this case, a silver-based material is incorporated within and throughout the PVC-U material ('Bio trunking'). The paper will provide an overview of the antimicrobial properties of silver, the microorganisms of particular concern and the methods used to assess effectiveness of the antimicrobial properties in the intended situation.

Attached microorganisms: a particular mode of existence

The study of microbiology had tended to focus on the properties of microorganisms suspended in liquid. The test-tube in the laboratory would be an example of this. However, more recently, it has been recognised that the majority of the planet's microorganisms exist attached on surfaces. If they are able to grow on these surfaces, then they form layers of growth known as biofilms.[1]

Biofilms are more common at solid-liquid interfaces, for example in a water pipe, on a tooth surface or on a catheter, where the liquid flows over the surfaces, bringing nutrients to the biofilm, removing waste products and transporting parts of the biofilm 'downstream', where they may attach to and colonise another surface.

Biofilms are complex structures, containing very high numbers of microorganisms (dental plaque contains 100,000,000,000 cells per gram). An additional problem is that attached microorganisms in biofilms are more resistant to antibiotics and other biocides than those which are floating around. This is a significant problem in medical device infections and wound infections.

On surfaces that are exposed to the air (i.e. at a solid-air interface), attached microorganisms are only able to multiply if sufficient moisture and nutrients are present. If multiplication occurs, then the possibility of biofilm formation and a detrimental effect on the appearance of the substratum emerges. Stains, odour and accumulation of 'dirt' in scratches or joints provide, at the very least, an unaesthetic appearance and also an increased biotransfer potential.[2,3] Thus the impregnation of an effective antimicrobial agent throughout the surface (rather than as a coating alone) should be advantageous, should any defects or damage occur.

In the absence of growth, survival is a possibility. Here, the microorganisms remain alive, quite possibly for several months, but do not grow. They are then able to grow when they are transferred to another, more favourable environment. Therefore it is important to reduce this survival as much as possible by cleaning to remove any attached cells and, by disinfection, to kill any that remain. Any antimicrobial surface treatment should provide additional protection when combined with normal and appropriate cleaning procedures[4], i.e. it should not be deemed sufficient for infection control or hygienic status to merely provide a treated surface.

At a solid-liquid interface, the antimicrobial may diffuse into the liquid and exert its effect (e.g. wound dressings, catheter treatments). At a solid-air interface, this is not possible: thus the effect must be exerted by direct contact between the agent and the target site in the attached microorganism. Bio trunking provides a durable, no-leaching antimicrobial treatment, with 'proven silver ion-based technology to neutralise any bugs with which it comes into contact'.

Silver as an antimicrobial agent

Silver has a long history of medical use, particularly in the treatment of wounds. This interest in its inclusion in wound dressings has continued to the present day with a very significant literature on the topic. Topical application (i.e. applying to a surface) is, however, different from using a treated surface, since access of the agent to the target organisms is direct, with the antimicrobial activity achieved via moisture present.

Elemental silver (Ag^0)appears to have little, if any, antibacterial action or ionic charge, whereas 'silver ions' are highly reactive. [Electrons can be lost from metals and the resultant metal ion is positively charged, a cation (Ag^+)]. An 'oligodynamic' effect has been proposed because of its ability to exert a bactericidal effect at very low concentrations. Unlike antibiotics, which have specific targets present in microbial cells thus demonstrating 'selective toxicity' (e.g. bacterial cell wall, targeted by penicillins), silver, like other biocides, is toxic to multiple components of bacterial cell metabolism. These include damage to the bacterial cell wall and membrane permeability.

The membrane is important in maintaining the internal environment of the cell: damage leads to blockage of transport and enzyme systems, alterations of proteins, particularly through interaction with sulphydryl groups (sulphur containing components of proteins) and binding of microbial nucleic acid, which prevents protein synthesis and cell division.[5,6,7]

Silver is soon inactivated by protein binding but this can happen outside the cell as well as inside the cell (e.g. in tissues if used as wound dressing or on a dirty exposed surface).[6,8] Thus rapid or sustained release is important – as could be demonstrated by impregnated surfaces where the silver is mobile and essentially renewable to the surface. Coatings might, in contrast, be lost or exhausted more rapidly.

Resistance is unlikely because of the several different bacterial cell systems that are affected.[5,9] The microorganisms would have to become resistant to all the different ways in which silver exerted its effect. There is, to date, little evidence of resistance, although repeated exposure to low levels might make resistance possible.

The lack of selective toxicity shown by silver means that its target cells are diverse: there is a 'broad spectrum' of activity. In clinical use, there is some concern over silver toxicity[6,8] although this is outweighed by the significant antimicrobial effect at low concentrations and could point to a use of silver in the immediate external environment, focused towards infection control and hygiene with reduced usage in terms of time applied to wounds.

Much focus is directed towards antibacterial activity but the broad range of activity extends to other microorganisms, with fungicidal (including yeast) activity as well as activity against protozoa and algae being demonstrated. Some antiviral activity has also been described.

Application of silver ions was most well-known via the use of silver nitrate as an eye-drop formulation to prevent newborn babies acquiring an eye infection (ophthalmia neonatorum) from mothers infected with gonorrhoea. Solid silver nitrate was used in a rod-shape to dab wounds. Silver foil was applied to burns.[10]

For treated articles and surfaces that will be exposed to microorganisms in the open air, it is important to ensure that some ionic activity is present. This may be via cleaning, where the moisture provided by the cleaning protocol would help 'activate' the silver but also moisture will be present in the cells themselves, which will be attached onto the surface in the presence of other organic material (sweat from fingerprints, blood, urine, faeces etc) where moisture may again be retained for some period of time. It is difficult to quantify such low levels of moisture in the laboratory when developing tests to demonstrate effectiveness.

Demonstrating effectiveness

The most effective visual used to illustrate an antimicrobial agent, be it antibiotic, toothpaste or essential oil, tends to be the 'zone of inhibition'.[11,12]

Here, microorganisms are plated onto agar and exposed to the putative agent, which is usually placed centrally on the agar plate. During incubation, the antimicrobial agent diffuses from its origin, setting up a concentration gradient (decreasing concentration away from the origin). The microorganism will grow as long as it is not killed or inhibited by the agent. Thus a large zone of inhibition (i.e. no growth over a wide radius) demonstrates high sensitivity to the agent; no zone represents resistance. However, the use of such images is inappropriate and misleading if the agent is intended to remain within the intended surfaces (i.e. does not diffuse).

It is extremely difficult to model systems, where kill by contact in a relatively dry environment is intended and where transient contamination of open surfaces is the key problem, in order to demonstrate clearly the effect of the antimicrobial surface treatment on the viability of the attached cells.

ISO 22196:2007 (JIS Z 2801:2000) attempts to simulate this phenomenon by monitoring the survival of known numbers of microorganisms on the test (and control) surface.

The cell suspension is maintained in contact with the surface via a polymer film, within a humid environment. Viability is assessed after a fixed time period. The surviving microorganisms are removed from the surface and the film. The resultant cell suspension is plated onto nutrient agar so that viable cells multiply to form colonies. One viable cell will form one colony, so that by counting the number of colonies the effect of the treated surface can be compared with the results from the control surface.

Bio trunking surfaces have demonstrated a greater than 99.9% kill rate using this method against MRSA (Methicillin resistant *Staphylococcus aureus*) and *Klebsiella pneumoniae*. These two bacteria are often used in these tests because they have different structural cell properties and also because they are important in the hospital environment. MRSA is well known as an antibiotic resistant, opportunist pathogen that can survive on surfaces within the hospital environment. It can colonise both healthy and sick individuals and is a significant problem in HCAI. It has also been associated with outbreaks of infection, thus transfer of the bacterium between individuals must be occurring. *K.pneumoniae* is also an opportunist pathogen important in the hospital environment.

It is possible to increase the challenge provided to the surface by supplementing the microbial inoculum with additional organic material such as protein, abrading the surface and examining the surfaces microscopically subsequent to the test for the presence of residual viable cells.
(N.B. Up-to-date and accessible information on a range of different pathogens, and their importance to public health can conveniently be found on the Health Protection Agency website www.hpa.org.uk.)

Profile of antimicrobial activity

Other bacteria against which Bio trunking has demonstrated effectiveness and which are listed in promotional material (although the specific test used is not noted) include:

- *Streptococcus pyogenes:* tonsillitis, scarlet fever, necrotising fasciitis (the 'flesh-eating bug').
- Vancomycin-resistant *Enterococcus faecalis*: *E.faecalis* is a fairly common opportunist pathogen, which becomes more of a concern when antibiotic resistance is acquired.
- *Escherichia coli:* All of us are colonised by *E.coli* in our gut but this bacterium can cause infections if it is transferred to a wound or a different part of the body. *E.coli* O157 is one type of *E.coli* – as MRSA is one type of *S.aureus* – but it is a true pathogen, rather than an opportunist, causing severe food-associated illness.
- *Pseudomonas aeruginosa*: a common bacterium found in water and other environments. It is an opportunist pathogen, being associated with biofilm development, burns infections and medical device infections as well as food spoilage.
- *Acinetobacter baumanii*: similarly versatile in its habitats. It is also associated with hospital acquired infection and is often resistant to many antibiotics.
- *Bacillus subtilis* is a spore forming bacterium. It is not particularly pathogenic but the ability of some bacteria to form resistant spores is a problem for cleaning and disinfection.
- *Salmonella:* the *Salmonella* species cause food-borne illness.
- *Legionella:* Legionellosis is a severe form of pneumonia caused by inhalation of infected aerosols, for example via air conditioning systems. The *Legionella* bacteria are believed to colonise biofilms within the distribution systems.
- Lactobacilli are essentially non-pathogenic: they are often used as probiotics. Some species cause spoilage, for example in the brewing industry.
- *Corynebacterium pseudodiphtheriticum:* another opportunist pathogen, associated with respiratory infection, with a slightly different cell wall structure than the other bacteria listed above.
- *Clostridium difficile*: a major problem in HCAI. C. difficile is an anaerobic organism that generally resides in the gut. It does not survive as a live organism in an oxygen atmosphere, either dying or changing into an inert spore. Bio trunking has not been demonstrated to be effective against *C.difficile*.

(NB. The Latin names of bacteria are usually italicised. The full name is used on first mention, e.g. *Escherichia coli* but the name is abbreviated in subsequent usage, *E.coli*. The species name (second name) e.g. *coli*, does not have a capital letter).

The more general acknowledgement of silver as a non-toxic antimicrobial agent has led to its incorporation into a wide range of inert materials with health or hygiene claims being overt or implicit: mobile phone covers, toilet seats, toys, socks and so on.

The data substantiating such claims are not always present or valid or convincing - if present at all.[9] It is important to ensure that appropriate tests are used to demonstrate an antimicrobial effect, effective at the intended point of use, so that claims made are accurate. Thus promotional literature for Bio trunking states that 'antimicrobial treatments provide an extra level of protection when combined with normal cleaning procedures'.

Professor Joanna Verran
January 2009

Some selected references:

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[12] Furno, F, Morley KS, Wong B et al. 2004. Silver nanoparticles and polymeric medical devices: a new approach to prevention of infection? J Antimicrob Chemother 54:1019-1024.

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Summarising points:

For consumer and environmental safety, particularly within a healthcare environment, the provision of cable management trunking that can, at one and the same time, be easily cleaned whilst still providing constant antimicrobial protection, will help reduce the transfer of micro-organisms.

- **CLEANABILITY:** the importance of a trunking system with rounded edges, smooth jointing, and a colour that enables visible dirt to be easily detected are prime considerations.

- **HYGIENE:** the incorporation into the trunking system of an antimicrobial agent provides one solution.

- **MICRO-ORGANISMS:** Micro-organisms left to grow on any surface risk being transferred to
  - human skin (e.g. the common cold)
  - wounds (e.g. MRSA)
  - food (e.g. *Salmonella* and *Listeria)*.

- **EUROPEAN BIOCIDAL PRODUCT DIRECTIVE:** any technology that addresses the problem of incorporating antimicrobial properties with its product must meet the requirements of the European BPD.

- **HOSPITAL ENVIRONMENT:** in a hospital environment, patients are particularly susceptible to infection, so reduction in the transfer of microorganisms directly via inanimate objects is a key objective.

- **OTHER ENVIRONMENTS:** in schools, sports and health centres, the presence of easy to clean surfaces coupled with additional antimicrobial properties may help reduce the transfer of microorganisms associated with colds and other respiratory infections or wound and skin infections, from person to person via surfaces.

- **SURFACE TREATMENT:** it is possible for microorganisms to remain alive, without growing, quite possibly for several months, only beginning to grow when they are transferred to another, more favourable environment. It is important to reduce this survival as much as possible by cleaning to remove any attached cells. It is not sufficient for infection control or hygienic status merely to provide a treated surface.

- **INTEGRAL TREATMENT:** if multiplication occurs on surfaces that are exposed to the air, with the increased risk of biotransfer potential, the impregnation of an effective antimicrobial agent throughout the PVC-U (rather than as a coating alone) should be advantageous if any defects or damage occur.

- **SILVER:** Silver has a long history of medical use, particularly in the treatment of wounds:
  - Silver is toxic to multiple components of bacterial cell metabolism, including damage to the bacterial cell wall and membrane permeability.
  - Damage leads to blockage of transport and enzyme systems, alterations of proteins and binding of microbial nucleic acid, which prevents protein synthesis and cell division.
  - Silver is soon inactivated by protein binding but this can happen outside the cell as well as inside the cell (e.g. in tissues if used as wound dressing or on a dirty exposed surface).[6,12] Thus rapid or sustained release is important – as could be demonstrated by impregnated surfaces where the silver is mobile and essentially renewable to the surface. Coatings might, in contrast, be lost or exhausted more rapidly.

- **BIO TRUNKING SOLUTIONS:** surfaces have demonstrated a greater than 99.9% kill rate using this method against MRSA (Methicillin resistant *Staphylococcus aureus*) and *Klebsiella pneumoniae*.
  - These two bacteria are often used in these tests because they have different structural cell properties and also because they are important in the hospital environment.

- **ISO:** Bio Trunking Solutions are tested to ISO 22196:2007 (JIS Z 2801:2000).