Combining copper with effective hygiene

Copper – for many centuries known for its antimicrobial properties – is increasingly being used in hospitals and other healthcare facilities worldwide as an aid to infection control and reducing healthcare-associated infections. Here Tim Sandle, head of Microbiology at Bio Products Laboratory, discusses how antimicrobial surfaces incorporating copper can assist with hospital infection control programmes and the fight against nosocomial infection.

Antimicrobial copper touch surfaces installed at Grinnell Regional Medical Center, US.

Infection control is concerned with eliminating as many pathogenic microorganisms as possible and limiting their transfer. This covers a range of measures – from handwashing and disinfection to selection of antimicrobial drugs, and treatment of surfaces.[1] With surfaces, many types of microorganisms can persist for extended periods of time (some organisms can survive for longer than 30 days on standard surfaces);[2] consequently touch-surfaces represent risk spots for pathogen transmission. In the hospital setting, some types of key equipment can be manufactured with antimicrobial touch components with the aim of making the surfaces self-disinfecting. For this a recent trend in the hospital setting has been to revisit the inherent antimicrobial properties of certain metals. A prominent example is the use, or incorporation of, copper.[3]

Contamination transfer

There are different means by which the pathogens responsible for hospital-acquired infections (HAIs) can be transferred.[4] One of the most common means is contact transmission (such as, by touch or from surfaces), either indirectly by healthcare professional to the patient, or from direct contact by the patient.[5] Other means include droplet transmission (when droplets are generated from the source person, mainly during coughing, sneezing, and talking); airborne transmission (which occurs by dissemination of airborne droplets containing microorganisms that remain suspended in the air for long periods of time); via dust particles containing infectious agents, which can be dispersed by air currents (e.g. during bed-making) and may become inhaled, and substances or materials, where contaminated items such as food, water, medications, or devices come into contact with the patient.

The seriousness of an HAI is linked to patient risk factors, such as the overall health of the patient, or by the means of contact, such as when invasive devices are used to break the patient's skin or enter the body through an orifice. A second factor affecting the seriousness relates to the microorganisms themselves, especially those with developed resistance to one or more antimicrobial drugs.[6] In relation to the subject of this article, surfaces can facilitate the development of resistance for some bacteria when deposited onto a surface, and which can survive exchange genes, including those for antibiotic resistance.[7] Thus standard surfaces can lead to the emergence of new, resistant strains.

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Antimicrobial surfaces

Control of surfaces as vectors for pathogen transmission is increasingly forming part of the overall infection control strategy. Considerable research has gone into finding ways to minimise the spread of infection, and much of this, as this article focuses on, is via the use of copper-based antimicrobial surfaces.

Copper: an historical antimicrobial

Metals such as copper have been used for their antimicrobial properties for thousands of years, including for water disinfection and food preservation, as practiced by Phoenicians, Greeks, Romans, and Egyptians.[8] While such knowledge never disappeared, the use of metal alloys in hospitals was either replaced by plastics and fabrics, or, where required, stainless steel (this metal has no antimicrobial properties). Therefore antimicrobial metals like copper have not played a significant part in the design and construction of healthcare facilities, at least until recently.

Copper and copper alloys (such as brass, cupronickel, copper-nickel-zinc, and bronze), are inherently antimicrobial. Experimental data shows copper possesses a rapid, broad-spectrum efficacy against bacteria and viruses, and it can kill viral pathogens such as influenza A and norovirus (surfaces containing 60% or more copper are especially effective);[9] as well as bacteria like *Escherichia coli*, methicillin-resistant *Staphylococcus aureus* (MRSA), carbapenem-resistant Enterobacteriaceae (CRE), and vancomycin-resistant enterococci (VRE). Such effects have been demonstrated under varying conditions of temperature and humidity.[10] Studies have additionally assessed the continuation of the antimicrobial effect after prolonged periods of time, and found no loss of activity, even when a copper-based surface is subject to regular cleaning.[11]

The precise mechanisms of action are a continuing subject of research, and the processes are complex and often interactive. The mechanisms of microbial kill can involve the release of copper ions from surfaces, although the quantities are extremely small. Depending upon the species, direct contact with a microorganism firstly instigates catalytic reactions that generate reactive oxygen species, which in turn damage the bacteria. Ions, once released, can enter the cell and cause protein dysfunction or membrane damage, affecting several cell targets, and killing the organism.[12] Recent work has shown that in the final stages of cellular reaction, bacterial or viral genetic material is completely destroyed, therefore limiting the potential for Horizontal Gene Transfer (HGT) conferring resistance between species to many classes of antimicrobials.[13]

As well as a direct effect, other data suggests that non-copper surfaces adjacent to those containing copper can also benefit, due to a 'halo effect.' Research conducted at the neonatal intensive care unit (ICU) in the Aghia Sofia Children's Hospital in Greece found that, as well as contamination being 90% lower

Antimicrobial hard surfaces – testing standards

Materials that can be manufactured into useful hard and touch surface components have entered the arsenal of those interested in healthcare-associated infections (HCAIs or HAIs), antimicrobial resistance (AMR), and, more recently, healthy building schemes. Silver was probably the first material to raise the possibility of reducing background contamination and the risk of HCAIs, but copper has received much more attention of late. This has led to new insights into the role of the environment in these issues.

When deployed correctly, certain materials have been shown to reduce pathogen (or more generally, bioburden) levels even when used in critical areas such as intensive care units, where cleaning is enhanced and traditional chemical disinfectants are regularly used. Liquid disinfectants are applied to a surface in order to inactivate or reduce the number of pathogenic microorganisms; they are more effective following cleaning (which has itself been shown to reduce microbe numbers significantly).[1] However, their use is limited by the time for which they are effective: as soon as a new contamination event occurs, the bioburden starts to rebound. Residually active disinfectants are being developed to extend effective times, but these may be potent chemicals that have unknown environmental implications.

Methods of testing

While a number of tests for liquid disinfectants have been developed over the years, the ability to reliably test new hard surface technologies has arguably not kept up with the promise of this new understanding. For many years, the only recognised test method for antibacterial materials designed to be made into components was a Japanese industrial standard, JIS Z 2801. This methodology was developed in the 1950s to evaluate plastics and foams with silver additives and was - and remains - the basis of marketing claims for such products. Subsequently, the method formed the foundation of an international standard, ISO 22196. These methods require the sample to be maintained in a wet condition of >95% humidity under a plastic film (the JIS test is colloquially known as the 'seal test') and tested at 35˚C. The logic of the original approach is that these conditions favour the survival of the bacteria, i.e. are a close approximation of their preferred *in vivo* conditions. When interest in antimicrobial hard surfaces for use in buildings increased in the 1990s, it soon became clear that the JIS/ISO methodology was not appropriate as a test to evaluate efficacy in ambient, indoor conditions.

The Organisation for Economic Co-operation and Development (OECD) established a working group to investigate these materials and propose a roadmap of testing and comparison. In 2008 OECD proposed a tiered testing system: Tier 1 being a simple 'proof of principle' test, into which the JIS/ISO method falls; Tier 2 tests closely approximating typical in-use conditions; and Tier 3, field tests.[2] Copper alloys were the first materials to be evaluated after the tiered system was proposed. In conjunction with the US Environmental Protection Agency (EPA), and experts from the Association for Professionals in Infection Control and Epidemiology (APIC) and the American Society for Healthcare Environmental Services (ASHES), a set of tests was developed that simulated a typical small splash contamination event, including recontamination and rubbing. Testing under these conditions verified that chemical and silver-containing composites did not show efficacy - they behaved similarly to the stainless steel control. Copper alloys showed rapid and complete inactivation of a range of bacteria.[3,4]

Some nations have adopted the tests established with the EPA, and the basic test has been 'Europeanised' as an industry best practice document, available on the antimicrobialcopper.org website. The EPA has subsequently revisited testing methods in the light of the development of composite materials and coatings, which have not shown adequate or long-term effectiveness. The EPA is currently consulting on methods that would effectively identify and reject materials with sub-lethal dose issues or no long-term efficacy.

In Europe, the British Standards Institute (BSI) is now leading the way in developing Tier 2 test methodologies, and hopes to finalise these in 2018.

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on copper alloy surfaces, these surfaces also exert some antimicrobial effect on non-copper surfaces up to 50 cm away, albeit with a reduced efficacy, reducing typical contamination to around 70%.[14]

Innovations with the use of copper in the healthcare setting

In the hospital setting, various studies have indicated that reductions in bacterial bioburden and infection rate can occur in rooms equipped with just a few copper surfaces, provided these surfaces are in appropriate locations.[15] In some studies, surface contact killing has been observed at a rate of seven to eight logs per hour, with no surviving organisms after several hours of contact.[16] In 2010, for example, a study undertaken at Selly Oak Hospital in Birmingham replaced particular fittings with copper alloys. These were used in an experimental composite toilet seat, as well as in other key items such as brass tap handles and door push plates. Collected data showed bacteria recovered from surfaces of copper-containing items were at levels 90%-100% lower than those from equivalent surfaces made from plastic or aluminium.[17] Such clinical trials led to the acknowledgement of the importance of reduced environmental bioburden in the NHS' EPIC3 guidance.

Based on such evidence, many hospital facilities have used copper or copper alloys for touch surfaces such as door handles, call buttons, toilet seats, IV poles, tables, stretcher rails, bathroom fixtures, and bed rails. Moreover, the use of copper need not be restricted to solid surfaces, for some manufacturers have developed copper oxide–impregnated textiles for use with bedsheets, pillowcases, shirts, pants, gowns, towels, underpads, and robes (intended for both patients and healthcare workers). Other sites have, in addition to the ward, upgraded different surfaces in the consultation room.

Antimicrobial copper door furniture at the Sir Robert Ogden Macmillan Cancer Centre, UK.

To apply antimicrobial copper to surfaces in the healthcare setting there are two options:

- Permanently 'manufacture in' an agent with antimicrobial activity like copper or copper alloy (some research has begun with copper composites, but the results are so far inconclusive).
- Periodically apply an agent with antimicrobial activity (e.g. copper-containing liquid agents or lacquer).

Here copper containing coatings may be lower cost than solid copper and offer broadly similar short-term antimicrobial properties.

An important question is whether the second approach is technically feasible? As it stands there is greater certainty in terms of antimicrobial properties from permanently manufactured surfaces.

The most cost-effective way of introducing copper alloys is to design them into the environment as ward components or parts of critical equipment such as bed rails. Some equipment is already available, such as a range of door furniture, drip poles, and keyboards. Realistically, given the current state of the market, only a few bed manufacturers have been willing to re-invest in tooling to accommodate this innovation.

With examples of the former – manufacturing from scratch – several companies have commercialised equipment and devices. For instance, to reduce the risk of hospital staff transferring contamination, a US company produced an antimicrobial copper keyboard. As well as the copper-based surface killing bacteria on contact, the keyboards can be cleaned and disinfected at regular intervals without loss of activity. A newer intervention is the commercial manufacture of copper alloy pens – an example of an item regularly passed around between personnel.

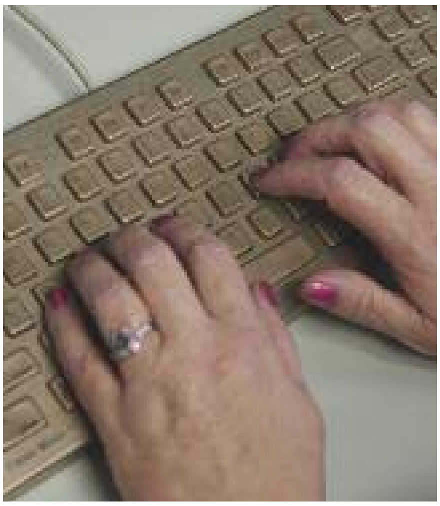
Alongside the manufacture of new copper-based surfaces, existing surfaces can be treated. Copper-based coatings can, in theory, be applied to a variety of substrates, such as plastic, ceramic, or metal, using conventional techniques such as spraying or dipping, and cured thermally or photochemically. These processes are, however, unproven in terms of antimicrobial efficacy, and especially longevity, in the hospital setting.

Where components cannot be permanently rendered with copper, copper can be applied as a sheet. For example, in the recreational setting, such as rest-rooms, some hospitals (and other locations) have fitted copper cupboard doors to kitchen facilities, and installed antimicrobial copper table tops.

As well as surfaces, airborne pathogens remain a risk. Here the application of copper can be beneficial. Technologists have considered the efficacy of copper in reducing contamination in heating, ventilation, and air-conditioning (HVAC) systems. HVAC equipment is used to cool hospital air, and it can also be used to create clean spaces, as with an operating theatre. With HVAC systems aluminium components are commonly used. Depending on design and the challenge from outside air, these components can encourage the development of stable biofilms of bacteria and fungi. The risk from this is that contaminants accumulate on heat exchanger coils and fins, in condensate drain pans, on air filters, and in air ducts. In contrast, the antimicrobial properties of metallic copper can limit the bacterial load associated with the copper heat exchanger fins.[18]

Resistance

Despite empirical data showing the success of copper in effectively killing a range of pathogens associated with healthcare-acquired infections, some organisms can exhibit resistance to copper, and this resistance can develop within microbial populations. There are various mechanisms by which bacteria can exhibit resistance. These include: extracellular sequestration of copper ions; having an impermeable membrane to copper ions; possessing copper-scavenging proteins; and undertaking the active extrusion of copper from the cell. Some strains of *E. coli* can, for instance, exhibit the latter mechanism.[19] However, these resistance mechanisms are only found when bacteria are subject to low doses of copper, e.g. as copper compounds found in agriculture or farming, and when sub-lethal doses may be taken up by microbes on low copper-containing composite materials. A better terminology would be to use the term 'tolerance' when considering such mechanisms. All tests to date show that these pathogens are rapidly overwhelmed when placed on copper alloy surfaces.



An antimicrobial copper keyboard.

Antimicrobial copper IV poles installed at Przyladek Nadziei, Poland.

Summary

This article has discussed how antimicrobial surfaces which use copper can assist with a hospital infection control programme and the fight against nosocomial infection. Data, both theoretical and empirical, has shown that replacing frequently-touched surfaces with antimicrobial copper equivalents, in conjunction with effective hygiene practices, can reduce pathogen numbers, lower the transmission of pathogens, and help to tackle antibiotic resistance in the hospital setting. **hej**

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