Contact Killing on Copper Surfaces:
From Lab to Application

PEER REVIEWED

As evidence grows for the key role of the environment in the spread of infection, the selection of materials for hygiene-sensitive environments is moving up the agenda, and copper is leading the way with unmatched efficacy against headline-making pathogens.

This article provides an update on the expanding evidence base – from laboratory experiments to clinical trials – and illustrates the growing adoption in healthcare and other sectors.

Proven Laboratory Efficacy

Copper is well-established as a powerful antimicrobial with rapid, broad-spectrum efficacy against bacteria and viruses, including MRSA, *E. coli* and norovirus. 'Antimicrobial copper' is the umbrella term for pure copper and the family of copper alloys – including brass and bronze – that benefit from the metal's inherent antimicrobial efficacy.

Copper's antimicrobial properties have been documented in scientific literature for more than a century, but it was not until 2000 that its efficacy against the pathogens responsible for healthcare-associated infections (HCAIs) began to be assessed. 15 years on, more than 60 papers report copper's efficacy against bacteria, viruses and fungi – hence the term *antimicrobial* rather than antibacterial or antifungal.

Antimicrobial copper touch surfaces work as an adjunct to existing infection control measures – such as hand-washing and regular surface cleaning and disinfection – which should continue as normal once copper is installed.

Claims of antimicrobial efficacy made for many antimicrobial products are based on JIS Z 2801 and ISO 22196 tests, conducted at >90% humidity, 35°C and over 24 hours under a plastic film. These basic tests are described as a proof of principle, and do not indicate how a material will perform in the field.

To better represent actual in-use conditions when testing copper, researchers developed new protocols to reflect typical room temperature and humidity, and used representative contaminants.

Laboratory research on the antimicrobial efficacy of copper and copper alloys has been carried out and verified at institutions around the world, with results peer-reviewed and published in respected journals. They exhibit efficacy under typical indoor conditions, unlike silver-containing materials and triclosan, which showed no antimicrobial efficacy under these conditions, as shown in Figure 1.[1]

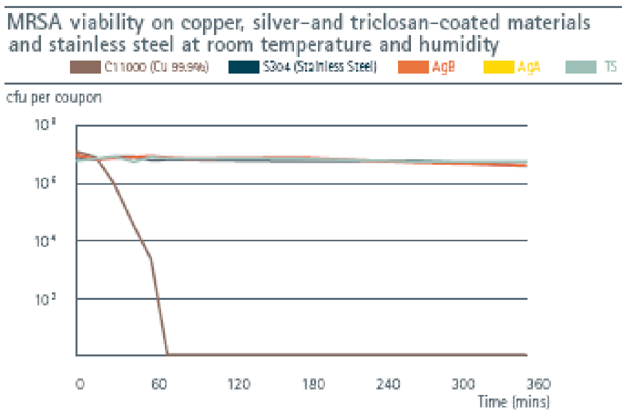

Figure 1 MRSA viability on copper, silver- and triclosan-coated materials and stainless steel at room temperature and humidity over six hours.[1]

Kill Mechanism

The exact mechanism by which copper kills bacteria – so called 'contact killing' – is still unclear, however several processes have been identified and research groups around the world are investigating, using different bacterial systems.

One proposed sequence of events is given below,[2] though it's worth noting that the sequence and importance of different steps may be different for Gram positive and Gram negative bacteria.

A. Copper ions dissolved from the copper surface cause cell damage.
B. The cell membrane ruptures, leading to loss of the cell content.
C. Copper ions lead to the generation of toxic radicals which cause further damage.
D. DNA becomes degraded and leaves the cell.

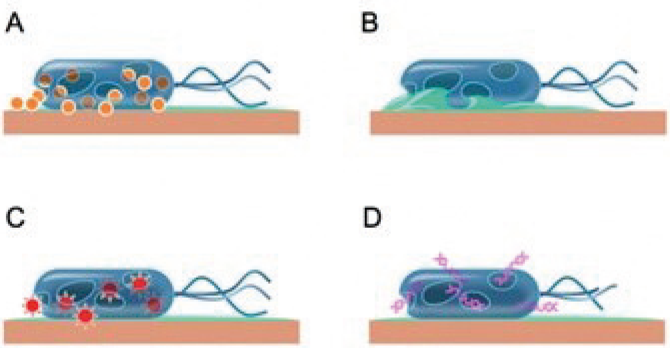

Figure 2

A Swiss research group investigated the role physical contact of bacteria with the copper surface has on contact killing.[3] They engineered special copper surfaces covered with an inert polymer mesh with holes of less than 1 micron diameter. This size is smaller than the test organism, *Enterococcus herae*, which meant the grid prevented the bacteria from making contact with the copper surface. They found that while the release of ionic copper was no different, the killing was reduced by seven orders of magnitude compared to untreated copper. They concluded that copper ion release and bacterial-metal contact were important for efficient contact killing.

Resistance is Futile

As bacteria evolve resistance mechanisms to antibiotics, the possibility of resistance to copper developing needs to be considered. This is considered highly unlikely for three reasons:

- Copper kills microorganisms by multiple pathways rather than by acting in a specific way on one receptor as do most antibiotics.
- Microorganisms are killed rapidly, before they can replicate, thus they cannot pass on genetic material which could ultimately lead to the development of resistance.
- Copper is naturally present in the earth's crust and, to date, no resistant organisms have been demonstrated. Copper-tolerant organisms do exist, but even these die on contact with copper surfaces. In comparison, resistance to penicillin by certain bacterial species began to appear within 30 years of its introduction.

Horizontal Gene Transfer

At the University of Southampton in the UK, a research team led by Professor Bill Keevil – one of the foremost experts on copper's antimicrobial properties – has demonstrated copper's efficacy against bacteria and viruses, including norovirus and Influenza A. They have also investigated the kill mechanism – with a recent focus on the DNA destruction – and investigated horizontal gene transfer (HGT) on copper and stainless steel surfaces.[4]

HGT in bacteria is largely responsible for the development of antibiotic-resistance, which has led to an increasing number of difficult-to-treat HCAIs. Professor Bill Keevil, Chair in Environmental Healthcare at the University of Southampton, explains: 'Whilst studies have focused on HGT *in vivo*, this work investigates whether the ability of pathogens to persist in the environment, particularly on touch surfaces, may also play an important role. We show prolonged survival of multidrug-resistant *Escherichia coli* and *Klebsiella pneumoniae* on stainless steel surfaces for several weeks. However, rapid death of both antibiotic-resistant strains and destruction of plasmid and genomic DNA was observed on copper and copper alloy surfaces, which could be useful in the prevention of infection spread and gene transfer.'

Copper's Role in Reducing HCAIs

A recent translational science article discussed copper alloys as antimicrobial environmental surfaces, summarising the evolution of the evidence base for copper, from the laboratory to the clinical environment.[5] The paper included the results of the largest clinical trial to date, which assessed copper's efficacy in the most challenging of clinical environments: intensive care units

.

The multi-centre trial – funded by the US Department of Defense – took place in the ICUs of three hospitals and aimed to answer the question 'Will the bioburden reduction associated with the installation of copper surfaces reduce the number of infections?'

The trial team found that replacing just six key, near-patient touch surfaces reduced the incidence of infections by 58%.[6] Figure 1 shows the accompanying reduction in microbial burden on the six surfaces.[7]

Just 10% of touch surfaces were upgraded to antimicrobial copper, yet the impact was significant. This study is the first to report a correlation between environmental bioburden (whether in copper or control rooms) and the risk of acquiring an infection, and to show a reduction in that risk due to a minimal intervention with an effective antimicrobial material.

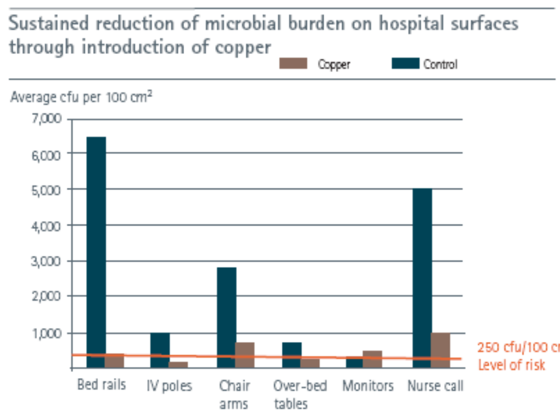

Figure 3 Sustained reduction of microbial burden on common hospital surfaces through introduction of copper. Proposed hygiene standard level is indicated in orange.[8]

Figure 3 demonstrates this correlation, with quartile distribution of HCAIs stratified by microbial burden measured in the ICU room during the patient's stay. There was a significant burden association between burden and HCAI risk, with 89% of HCAIs occurring among patients in rooms with a burden of more than 500 cfu per 100 cm^2.[6]

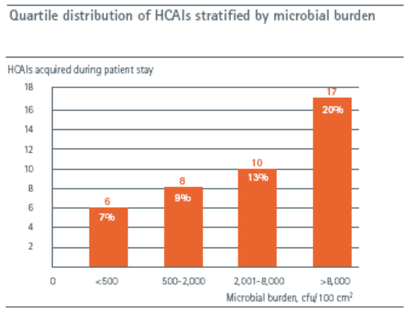

Figure 4 Quartile distribution of HCAIs stratified by microbial burden measured in an occupied US ICU room.

The trial found an 83% reduction in bacteria on copper alloy components in comparison with surfaces made of standard materials in the control rooms. This reduction corresponded to a 58% reduction in infection rates in patient rooms with components made of copper in comparison with patient rooms containing components made of standard materials.

The authors concluded: Bacteria die on copper alloy surfaces in both the laboratory and the hospital rooms. Infection rates were lowered in those hospital rooms containing copper components. Thus, based on the presented information, the placement of copper alloy components in the built environment may have the potential to reduce not only hospital-acquired infections but also patient treatment costs.

Does Copper Offer a Cost-effective Intervention?

Copper and its alloys are sometimes perceived as expensive, however they continue to be widely used throughout industry because they offer good value. Most of a component cost comes not from the intrinsic material value, but a combination of fabrication and fitting costs. Copper alloys are widely used for complex components – such as taps and locks – because they are easy to fabricate.

Fitting costs are broadly the same for any given component. Professor Tom

Elliott, leader of the Selly Oak research, has stated that 'the cost of fitting out the 20-bed trial ward was equivalent to the cost of just one-and-a-half infections.'

The US research group calculated the time to recoup the cost of installing the copper components.[5] They first calculated the cost difference between all the copper and standard components used in the trial (52,000 USD). Then, they calculated the cost savings made during the 338 days of the trial by saving 14 infections at 28,400 USD each (397,600 USD). This gave a daily saving of 1,176 USD, so payback was calculated as 52,000/1,176 = 44 days.

The calculation was based on the US cost of infections and the cost of copper components before they were commercially available.

York Health Economics Consortium (YHEC) – leading global health economists based at the University of York in the UK – developed a model to enable estimates of payback to be made for new builds or refurbishments. The model uses costs of infection in UK ICUs and a cost differential between copper and standard components based on recent industry data.

The model allows different infection reduction rates to be inputted. Using the US data (58% reduction in infections), payback is achieved within one month and a sensitivity analysis shows that even at 20% efficiency, payback is within two months.

The model's authors conclude: 'This is an engineering solution needing capital budget (typically held by Facilities/Estates) but with impact on infection prevention, cost of care and clinical outcomes. This therefore requires a high degree of understanding and collaboration at senior decision-making level.'

Awareness and Adoption

Key healthcare watchdogs and horizon-scanning bodies around the world – including ECRI Institute and The Canadian Network for Environmental Scanning in Health – have recognised the growing body of evidence for copper's potential to boost infection control. It has also been acknowledged in the UK's evidence-based EPIC 3 guidelines, which included copper as an emerging technology in 2014.[9]

Installations have taken place in hundreds of facilities around the world, with hospitals and clinics leading the way whilst care homes, schools, gyms, airports and train stations also incorporate antimicrobial copper touch surfaces to improve hygiene.

The first pharmaceutical facility to install copper is PharmaQ – a manufacturer and distributor of pharmaceutical products for the healthcare industry, based in South Africa.

PharmaQ's then CEO, Dan Breet, hit upon the idea of using copper to tackle problems with the bacterial load on packing tables in the laboratory, which was frequently inspected by officials from South Africa's Department of Health.

One side of a stainless steel packing table was replaced with brass, and microbial levels on this were compared with those on the other, stainless steel side. The average count of colony forming units was consistently and significantly lower on the copper, and PharmaQ is planning a presentation at a future pharmaceutical conference and further deployment of copper surfaces.

Laboratories are also harnessing the antimicrobial power of copper, with the latest example being an incubator at the University of Liverpool Biological Sciences Department in the UK. Preventing contamination within the incubator was a high priority, so they opted to install one with an antimicrobial copper lining, in addition to the standard HEPA filtration and a high-temperature decontamination cycle.

Availability

Copper alloys offer a wide palette of colours – from the gold of brasses to the rich brown of bronzes right through to the silver/white shades of copper-nickels. Copper alloys will naturally darken over time, but this does not impact their antimicrobial efficacy. More colour-stable alloys – traditionally used in naval applications – are also available.

The evidence base for copper is growing, in both lab and field tests, and this is now leading to adoption of antimicrobial copper surfaces by hospitals, care homes and other hygiene-sensitive environments. The supply chain is responding by continuously growing the range of antimicrobial copper products and alloy options available.

References

1. Michels, H. et al. 2009. Effects of temperature and humidity on the efficacy of methicillin-resistant Staphylococcus aureus challenged antimicrobial materials containing silver and copper. Letters in Applied Microbiology.
2. Grass, G. et al. 2011. Metallic Copper as an Antimicrobial Surface. Applied and Environmental Microbiology.
3. Matthews, S. et al. 2013. Contact Killing of Bacteria on Copper is Suppressed if Bacterial-Metal Contact is Prevented and is Induced on Iron by Copper Ions. Applied and Environmental Microbiology.
4. Warnes, S.L. et al. 2012. Horizontal Transfer of Antibiotic Resistance Genes on Abiotic Touch Surfaces: Implications for Public Health. mBio.
5. Michels, H. 2015. From Laboratory Research to a Clinical Trial: Copper Alloy Surfaces Kill Bacteria and Reduce Hospital-Acquired Infections. Health Environments Research & Design Journal. 1–16.
6. Salgado, C.D. et al. 2013. Copper Surfaces Reduce the Rate of Healthcare-Acquired Infections in the Intensive Care Unit. Infection Control and Hospital Epidemiology.
7. Schmidt, M.G. et al. 2012. Sustained Reduction of Microbial Burden on Common Hospital Surfaces through Introduction of Copper. Journal of Clinical Microbiology.
8. Schmidt, M.G. et al. 2012. Sustained Reduction of Microbial Burden on Common Hospital Surfaces through Introduction of Copper. Journal of Clinical Microbiology.
9. Loveday, H.P. et al. 2014. Epic3: National Evidence-Based Guidelines for Preventing Healthcare-Associated Infections in NHS Hospitals in England. Journal of Hospital Infection.

Angela Vessey, Director of Copper Development Association in the UK, studied Physiology (BSc) at Bedford College, University of London, and Applied Immunology (MSc) at Brunel University.

Her early career was in medical research in the Immunology Division of the National Institute for Medical Research. She joined Copper Development Association – a non-profit trade association – in 1996 and became director in 2001.

In 2005, she initiated the Antimicrobial Copper programme to disseminate information and to work with industry to make efficacious products available for healthcare facilities.