A Winner Emerges in the War Against Microbes

PEER REVIEWED

Man has benefited from copper's inherent antimicrobial properties since the dawn of civilisation, yet it is only in the last 10-20 years that scientific studies have been conducted to properly evaluate the metal's potential in reducing contamination in critical environments such as hospitals and food processing facilities. In the healthcare sector, the level of laboratory and clinical evidence has stimulated demand for incorporating copper into touch surface hot-spots in the fight against healthcare-associated infections (HCAIs).

Hand hygiene is a pillar of infection control, but in recent years the less than adequate compliance displayed by healthcare workers – before patients and visitors are even factored into the equation – has led many hospitals to the conclusion that more needs to be done in the fight against healthcare-associated infections.

Significant reductions in certain HCAIs – such as MRSA and *C. difficile* – are encouraging, but current figures still show that, within the European Union, over 4 million patients contract an HCAI each year. Given these infections lead to upward of 16 million extra days in hospital, and account for an estimated 37,000 deaths while costing the NHS alone over £1 billion annually, it is clear a new approach is needed.

Copper – an essential element required by both plants and animals to live – is a very familiar metal thanks to its superior electrical and thermal conductivity, and its ability to alloy with other metals to produce important metals such as brass and bronze. This same metal that has been part of daily human life for thousands of years could also be part of the solution to HCAIs.

Professor Bill Keevil – now Chair in Environmental Healthcare and Principal Investigator (Microbiology & Environmental Health) at the University of Southampton – was the first researcher to demonstrate copper's ability to rapidly kill the bacteria that cause HCAIs. As he explains, even this application of copper is far from new to us.

"Since ancient times, mankind has been aware of the beneficial properties of copper to reduce microbial infections. Even though people did not understand the germ theory back then, they recognised the correlation between copper and disease protection. 5000 years ago, the Egyptians for example used copper to transport water and to heal wounds. Later on, in the 1850s, it was noticed that during Parisian Cholera outbreaks, the copper workers did not get affected."

Professor Keevil's work suggested a role for copper in the healthcare environment: if it was effective at killing bacteria as well as viruses and fungi in the laboratory setting, could it be used for frequently-touched surfaces in hospitals to continuously reduce contamination and help break the chain of infection?

This question was addressed by a clinical trial at Selly Oak Hospital in Birmingham, led by Professor Tom Elliott, Consultant Microbiologist for University Hospitals Birmingham NHS Foundation Trust. He and his team investigated whether copper – and specifically useful alloys that benefit from its antimicrobial efficacy, including brasses, bronzes and copper-nickels – deployed as touch surfaces such as grab-rails, door furniture, light switches, taps, overbed tables, sink-traps and toilet seats would result in significantly lower levels of contamination on these surfaces.

The results appeared in national and international media, and caught the attention of the international infection prevention community: with normal cleaning, the copper surfaces achieved a greater than 90% reduction in bioburden compared to standard, non-copper surfaces.

This remarkable reduction translates to a reduced risk of bacteria and viruses being passed between people via these surfaces, and consequently less chance of vulnerable patients acquiring life-threatening infections.

Professor Elliott recently observed: "Self-disinfecting surfaces such as copper are a significant step forward in reducing infection-causing microbial bioloads on clinical surfaces. We should now ask the question: why select a non-antimicrobial surface when we know that some naturally-occurring metals, such as copper, have this intrinsic antimicrobial activity?"

Indeed, copper and the alloys that share its antimicrobial activity – collectively termed 'antimicrobial copper' – are of great interest to companies looking to 'design out infection' to meet the growing market demand for effective antimicrobial surfaces, and a number of clinical trials around the world have supported the Selly Oak findings. Trials have reported from Japan, Chile and the US, confirming the significant reduction in contamination, and further trials are underway in France and Greece.

A recently completed US trial has gone beyond demonstrating bioburden reduction to look at impact on patient outcomes. Initial results, presented by trial leader Dr Mike Schmidt at the 2011 WHO International Conference of Prevention and Infection Control (ICPIC)[1], indicated a greater than 40% reduction in the risk of patients acquiring a hospital infection when in single ICU rooms where key touch surfaces had been replaced with antimicrobial copper equivalents.

The trial was conducted in three world-class facilities and funded by the US Department of Defense, and had three distinct stages.

In the first, the baseline microbial burden on frequently-touched objects in ICU rooms was established, prior to the installation of any antimicrobial copper items. The goal of this phase was to ensure the most effective deployment by identifying the most heavily contaminated surfaces. The most bioburden was found on bed rails (with an average 13,028 cfu per 100 cm^2)[2]. Also highly contaminated were over-bed tables, visitor chair arms, nurse call buttons, data input devices and IV poles.

The second stage was to replace these surfaces – which equalled around 10% of the room's total touch surface area – with antimicrobial copper items, and compare the microbial burden on these and non-copper equivalents over the course of 135 weeks. Weekly sampling was undertaken in the copper and control rooms, with colony-forming units and indicator organisms counted. The median bioburden found on copper surfaces was 97% less than that on the control surfaces[3].

The third and, perhaps, most exciting stage – reported at ICPIC – assessed incidences of HCAIs in the copper and control ICU rooms. This data was reviewed by hospital statisticians to ensure it was robust and the results were significant. Preliminary findings show a significant reduction in the risk of acquiring an infection in rooms where antimicrobial copper touch surfaces are present. The percentage reduction in risk is between 40 and 70%, and was described by the study team as a significant and consistent reduction in infection rates.

The reason for the variation was that certain items (such as chairs) travelled between rooms, and bariatric patients were not able to use the standard-sized antimicrobial copper-railed beds. The number of antimicrobial copper components in all the rooms was monitored throughout each patient's stay, and the preliminary results show that patients who were in a room with 75% of the antimicrobial copper components present (by surface area) had a 40.4% reduced risk of acquiring an infection. This risk reduction increased to 61% if the patient was in an antimicrobial copper-railed bed in a copper room, and for patients in rooms with all antimicrobial copper components present for the full duration of their stay, the risk reduction was 69.1%.

Trial leader Dr Mike Schmidt, Professor and Vice Chairman of Microbiology and Immunology at the Medical University of South Carolina, says of the results: "Bacteria present on ICU room surfaces are probably responsible for 35 to 80% of patient infections, demonstrating how critical it is to keep hospitals clean.

"The copper objects used in the clinical trial supplemented cleaning protocols, lowered microbial levels, and resulted in a statistically significant reduction in the number of infections contracted by patients treated in those rooms."

Alongside this research into the impact of antimicrobial copper in the clinical environment, scientists are seeking to further our understanding of how copper exerts its antimicrobial effect. The exact sequence is still under investigation, however several mechanisms exist that appear to work in concert, and these are being studied by research groups around the world. The currently-known mechanisms are:

- Causing leakage of potassium or glutamate through the outer membrane of bacteria,
- Disturbing osmotic balance,
- Binding to proteins that do not require copper,
- Causing oxidative stress by generating hydrogen peroxide,
- Causing degradation of bacterial DNA.

The multiple mechanisms and, in particular, degradation of bacterial DNA are highly significant when considering the long-term deployment of antimicrobial copper touch surfaces, as UK researcher Professor Keevil explains: "We know that copper kills viruses and destroys DNA, including plasmids, so this should stop the transfer of DNA which would include those toxic genes and also the transfer of antibody resistance from one species to another."

Convinced by the science, infection control professionals next question the price of installing antimicrobial copper touch surfaces. To address this concern, the International Copper Association (ICA) commissioned York Health Economics Consortium (YHEC) to develop a cost-benefit model to illustrate the economic rationale of an antimicrobial copper intervention. Using figures for a UK ICU, the model shows the antimicrobial copper surfaces pay for themselves in less than one year.

York Health Economics Consortium – a company wholly owned by the University of York – was established in 1986 to extend the University's services into the healthcare sector. It was selected for this project by ICA as it provides consultancy and research in health economics to the NHS and the pharmaceutical and healthcare industries, and was well-placed to develop a comprehensive and robust business model.

YHEC used the results from the clinical trials previously described as a basis for reductions in HCAIs achievable following a copper installation. The model is populated with referenced datasets for rates and costs of HCAIs, cost of antimicrobial copper components and similar non-copper components without antimicrobial efficacy. It also offers users the opportunity to enter their own local data to produce customised calculations.

Presenting a Master Class at the London Reducing HCAIs Conference in October, Mark Tur, Antimicrobial Copper Technical Consultant for Copper Development Association, explained the need for the business model: "The copper intervention is an engineering one: it's different to other measures being deployed to tackle HCAIs, like new procedures or consumables. It requires capital spend, but then delivers savings to care budgets. We're often asked about the cost of installing Antimicrobial Copper. The real question is about the value of copper, not the cost. This model will help infection control staff, who accept the science, convince their CEOs to look at implementing Antimicrobial Copper for any planned extensions or refurbishments. Payback in less than one year makes this an intervention that warrants their attention."

The payback times demonstrated by the model back the findings of Professor Tom Elliott, leader of the Selly Oak clinical trial. At an event earlier this year, he noted: "For the one-off cost of installing Antimicrobial Copper surfaces, you get continuous microbial contamination reduction throughout the products' life, and these materials are durable and long-lasting. The cost for a 20-bed medical ward was equivalent to the cost of just 1.5 infections."

The final report and model are due for completion later in the year, but an advance document detailing a worked example using actual screenshots from the software is already available on the antimicrobial copper website.

There is a stewardship scheme for antimicrobial copper, which is administered by the International Copper Association and a global network of centres that together form the Copper Alliance. This offers reassurance to those wishing to specify antimicrobial copper products that they are buying an efficacious product from a company that is aware of the requirements for supplying them, for example ensuring the product is uncoated, since any permanent or temporary coating would come between the active surface and pathogens, rendering it ineffectual.

A Products and Services Directory on www.antimicrobialcopper.org contains a list of approved companies.

The antimicrobial copper website also contains case studies of installations using antimicrobial copper touch surfaces as part of their infection prevention approach, which are taking place around the world. Some are outside the healthcare environment, in other facilities and high-traffic areas where the spread of infection is a concern. In Europe, the latest are Hagen General Hospital in Germany (installing antimicrobial copper door furniture throughout a children's ICU), Craigavon Area Hospital in Northern Ireland (who have copper surfaces in their trauma and orthopaedic facility, theatres and maternity and, most recently, in a new operating theatre suite) and NHS facility Homerton University Hospital (which installed antimicrobial copper during the renovation of a specialist Adult Rehabilitation Unit).

In Asia, Hua Dong Hospital in China, the Respiratory Intensive Care Floor has been extensively fitted with a range of antimicrobial copper surfaces. Ochiai Clinic in Japan also has a range of antimicrobial copper surfaces (in a striking brass that appealed to the architect) and elsewhere in Japan – beyond healthcare – three kindergartens (including two rebuilding in the Fukushima area) also have installations including antimicrobial copper taps, serving trolleys, work surfaces and stair rails.

South America has installations including Chile's oldest paediatric hospital, where the ICU is equipped with numerous antimicrobial copper surfaces including bed rails, taps, IV poles and medical clipboards. Congonhas Airport – one of Brazil's busiest transport hubs – has antimicrobial copper handrails and counter tops, and sections of the Chilean Metro also have antimicrobial copper handrails, with the plan being to gradually extend them around the network.

Table 1.

Bed rails	Door knobs	Sinks	Dispensers
Over-bed tables	Door push plates	Taps/faucets	Toilets
IV poles	Visitor chairs	Work surfaces	Trolleys
Grab bars	Patient chairs	Computer input devices	Linen hampers
Light switches & sockets	Bedside tables	Call buttons & pull cords	Wastebins

For hospitals, healthcare facilities and other areas in which infection prevention is a concern, installing antimicrobial copper touch surfaces is a straightforward process. The highest-risk surfaces have been identified by clinical trial teams around the world based on their experience, and confirmed by sampling and subsequent testing. The following table shows items identified in clinical trials as having the greatest bioburden, and thus the focus for those looking to implement antimicrobial copper.

The rapid antimicrobial efficacy of copper, demonstrated under typical indoor conditions of humidity and temperature, has highlighted the inadequacy of current test standards for antimicrobial materials, conducted at greater than 90% relative humidity and 35°C.

Standards bodies are now working towards more appropriate test methods which will support manufacturers' claims for their hard surface products. This realisation has been a major factor in component manufacturers switching to copper to differentiate their products, and a growing number are offering antimicrobial copper touch surfaces in their healthcare ranges.

As the level of awareness of the fundamental research into the efficacy of copper and its alloys rises, other sectors are also looking at how to harness this inherent property of copper to control problematic microorganisms with a whole range of durable, cost-effective and versatile copper alloys. In the war against microbes, copper is the clear winner.

References

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