# Copper, Pathogens and Disease

This resource looks at the antimicrobial properties of copper and how these are being harnessed to help prevent the transmission of the pathogens that cause healthcare-associated infections in hospitals. Below are different sections, for quick navigation.



**Antimicrobial Copper Live Demonstration**

Professor Bill Keevil demonstrates copper's powerful and rapid antimicrobial activity in his laboratory at the University of Southampton.

*Professor Bill Keevil's pioneering research at the University of Southampton paved the way for a modern understanding of copper's antimicrobial properties*

## What is an Antimicrobial?

An antimicrobial is an agent that kills microorganisms - bacteria, viruses and fungi (including moulds) - or inhibits their growth. Antimicrobials include antibiotics such as penicillin and disinfectants such as bleach (sodium hypochlorite). This resource describes the properties and applications of copper in solid form, as a surface material.

## Healthcare-associated Infections

A healthcare-associated infection (HCAI) is an infection that a patient develops in a hospital either as a direct result of medical or surgical treatment, or from simply being in that setting. The important criterion for defining an infection as an HCAI is that the patient did not have the infection when they were admitted to the hospital.

The spread of these infections affects hundreds of millions of people worldwide. They increase patients' suffering and prolong the length of stay in hospital. A growing number of bacterial HCAIs are resistant to the antibiotics used to treat them. This situation can be summed up by 'bad bugs, no drugs'.

HCAIs include those caused by meticillin-resistant *Staphylococcus aureus* (MRSA), meticillin-sensitive *Staphylococcus aureus* (MSSA), *Clostridium difficile* (C. difficile) and *Escherichia coli* (E. coli). HCAIs pose a serious risk to patients, staff and visitors, cost the NHS in excess of one billion pounds a year and cause suffering, as well as leading to death in some cases. Infection prevention and control is therefore a high priority for hospitals. The main pillars of infection control are hand hygiene and cleaning and disinfecting the hospital environment, to kill pathogens before they can be spread. New approaches are being developed including the use of antimicrobial materials in the environmental surfaces to boost infection control.


*A wide variety of items can be made from copper and its alloys. (Courtesy of Operator Interface Technologies.)*

## MRSA (Meticillin-resistant *Staphylococcus aureus*)

*Staphylococcus aureus* is a common bacteria that is found on the skin and in the nostrils of about a third of healthy people. Meticillin (previously known as methicillin) is a type of penicillin, an antibiotic that is used to treat infections. MRSA are types of *Staphylococcus aureus* that have developed resistance to meticillin and were first detected in the 1960s.

MRSA is a problem in hospitals as patients undergo surgery and invasive procedures such as insertion of intravenous lines, which provide the opportunity for bacteria to enter the body and cause infection. MRSA can cause skin infections such as boils or, in more vulnerable patients, more serious infections in wounds, bones, lungs and blood.

## Historical Uses of Copper for Hygiene

The Ancient Egyptians, Greeks, Romans and Aztecs used copper-based preparations to treat burns, sore throats and skin rashes, as well as for day-to-day hygiene. Greek soldiers are reported to have scraped the bronze from their swords into open wounds to reduce the likelihood of infection during battles.

In the 19th century, with the discovery of the cause-and-effect relationship between germs and the development of disease (Pasteur's Germ Theory), scientific evidence started to be gathered. In the last few decades, extensive research has been carried out on the antimicrobial properties of copper and its alloys against a range of microorganisms including those responsible for HCAIs.

# Laboratory Research

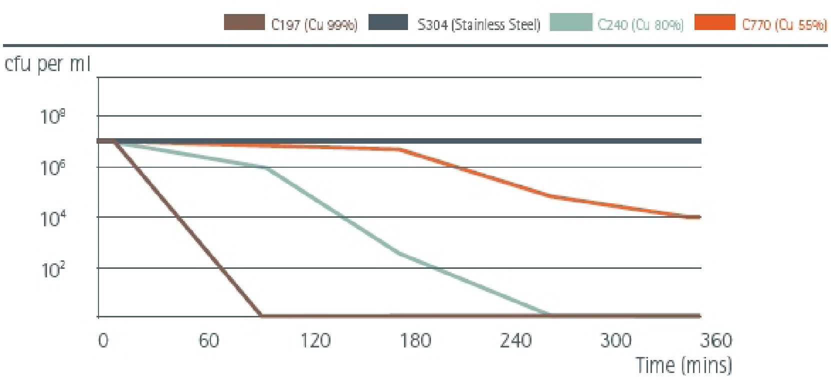
Laboratory tests have been developed to simulate contamination events under typical indoor temperature and humidity to measure the survival of bacteria on samples of copper and copper alloys such as brass and bronze.

The procedure is outlined below and simulates a splash or a sneeze landing on a surface:

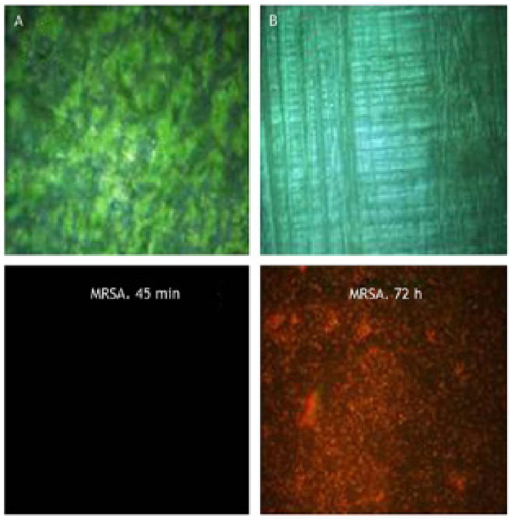
- 10 million bacteria are suspended in 20 µl of medium and spread across a 1 $cm^2$ coupon of test or control material. (note this is a far higher number of bacteria than would be seen in a typical contamination event in a hospital, to make this a challenging test).
- The coupons are placed in petri dishes and incubated at room temperature for different lengths of time.
- Surviving bacteria are recovered using glass bead vortexing and cultured for 48 hours in an incubator at 37° C and then counted by standard microbiological techniques.

The control is stainless steel, a material commonly used in hospitals but with no antimicrobial properties.

MRSA viability on copper alloys and stainless steel at 20˚C




This graph is the kill curve for MRSA on copper, brass (80% Cu,

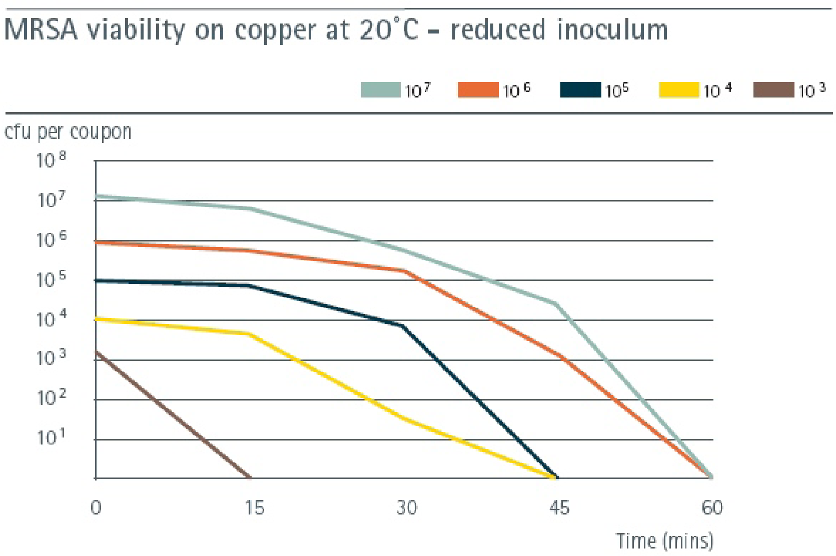



*Epifluorescent images of copper (A) and stainless steel (B) inoculated with MRSA. Following the exposure period (45 minutes for copper, 72 hours for stainless steel) the samples were transferred to petri dishes and incubated for two hours, then examined with epifluorescence filters. The red points on the stainless steel represent respiring cells. None remain on the copper.*

20% Zn) and nickel silver (55% copper, 27% zinc and 18% nickel) at $20^{\circ}$ C and typical indoor humidity. The vertical axis on the graph shows the concentration of colony forming units (cfu per ml ). There is complete kill in less than 90 minutes on copper. The two copper alloys also showed good kill rates but the kill times were longer and dependent on copper content. Note that even after 6 hours there is no reduction on the stainless steel coupon.

A similar protocol was used for extensive pass/fail laboratory testing as part of a United States regulatory registration process, where a >99.9% reduction of bacteria within two hours was required. Copper alloys with copper contents greater than 60% passed this test, as well as two even more demanding recontamination and wear tests, so this has become the minimum copper content for antimicrobial copper alloys.

The graph below shows how the kill time falls as the number of MRSA bacteria deposited on the copper surface reduces to more typical levels. A hospital door handle could have 1000 colony forming units (cfus) on its surface and these would be totally eliminated in less than 15 minutes. Because of the very high numbers of bacteria being investigated, these kill curves are shown with a logarithmic (log) scale, expressed as shown: $10^4$ is equivalentto 10,000.




*Copper has been shown to kill many other bacteria in tests such as this, and also to be effective against viruses such as Influenza A and Norovirus as well as fungi such as Candida albicans.*

*Sampling of a copper push plate at Selly Oak Hospital in Birmingham.*

## Clinical Trials

Having established the inherent ability of copper and copper alloys to eliminate bacteria and viruses in the laboratory, the next logical step was to discover how this would translate into real world environments and have practical application.

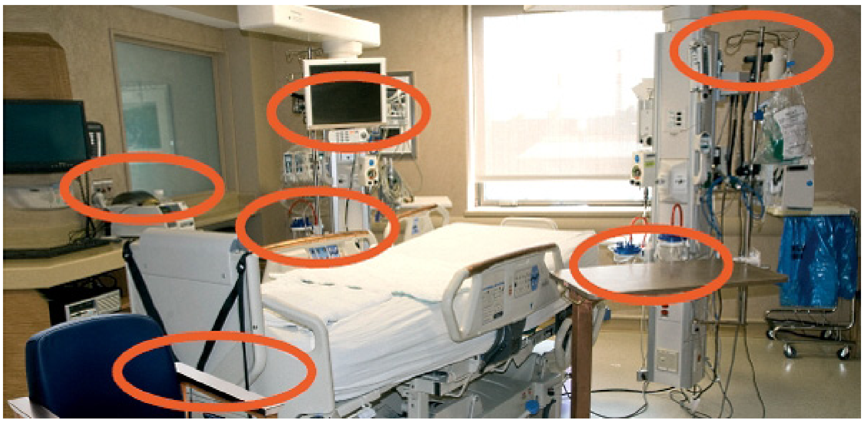
The first clinical trial was undertaken at Selly Oak Hospital in Birmingham, UK. The researchers replaced frequently-touched surfaces on a general medical ward - including over-bed tables, taps and door handles - with antimicrobial copper equivalents, measuring the contamination on these and comparing it with that on non-copper surfaces. The copper surfaces were found to have 90–100% fewer micro-organisms on them than the same items made from standard materials.

Trials in the US, Chile, Germany and Finland have supported the Selly Oak findings and verified that the effect is a continuous reduction in contamination - occurring 24/7 and in between regular cleaning.

The largest trial to date was a multi-centre clinical trial, funded by the US Department of Defense. The group identified the most heavily contaminated touch surfaces and upgraded them to copper in eight single intensive care unit (ICU) rooms. They then sampled these and standard components in eight control rooms regularly over two years and recorded the total bacteria recovered. They then reviewed the infections acquired by patients in the copper and control rooms.

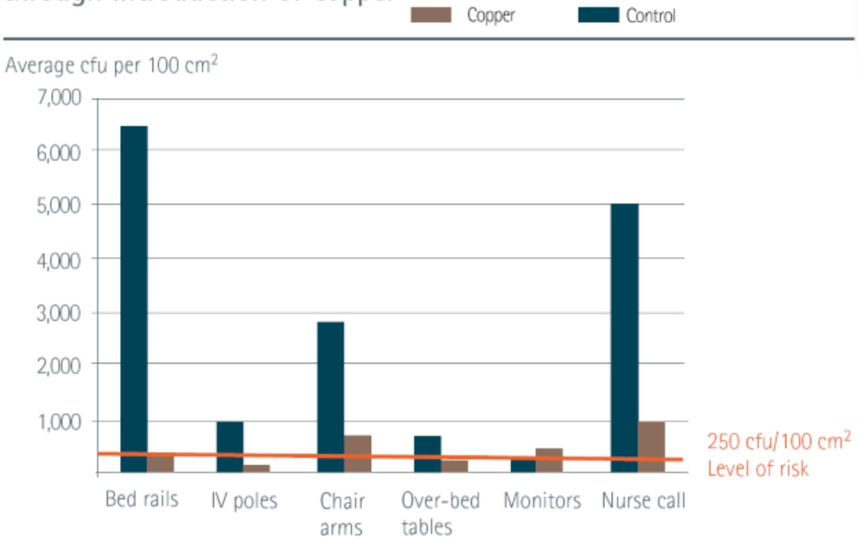
The surfaces identified as most contaminated were those closest to the patient:

- Bed rail
- Overbed table
- IV pole
- Computer input devices (mouse/monitor bezel)
- Visitor chair arms
- Nurse call button



*A copper-equipped bathroom at Isku Medical Centre in Finland.*

Sustained reduction of microbial burden on hospital surfaces through introduction of copper




This graph shows the number of bacteria found on these components in the copper and control rooms. The copper items had 83% fewer bacteria than the control items. Of all the bacteria recovered, only 17% were from the copper items. The proposed standard for a safe level of bacteria in hospitals is shown as a horizontal line in orange at 250 cfu/100 $cm^2$. There were 58% fewer infections in the copper rooms than the control rooms. This result challenges current thinking that the environment only accounts for 20% of infections.

From all the data collected it was possible to plot the infections acquired against the levels of bacteria for all rooms. These data show a strong correlation between levels of bacteria on these frequently touched surfaces and the risk of acquiring an infection. The trial leader, Professor Mike Schmidt, surmised that this emphasises the importance of the role of the environment in the transmission of infection.

## How does Copper Kill Bacteria?

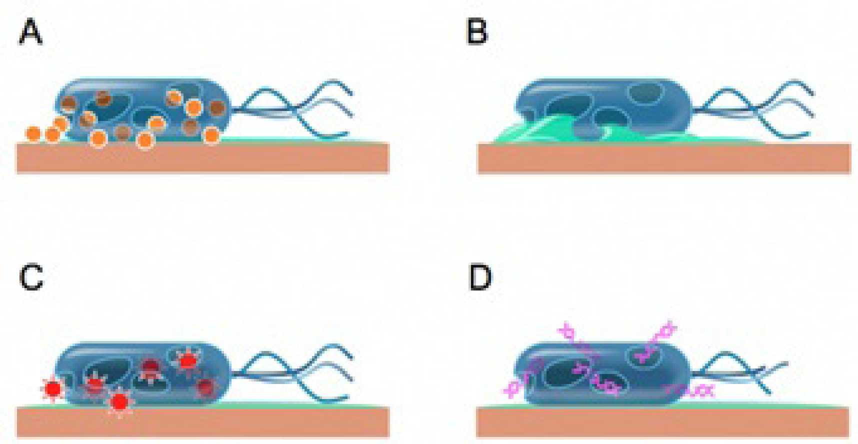
Copper is an essential nutrient for bacteria as well as humans but, in high doses, copper ions can cause a series of negative events in bacterial cells. The exact mechanism by which copper kills bacteria is still unclear, however several processes exist and are being studied. One proposed sequence of events is given below:

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 that cause further damage.

D. DNA becomes degraded and leaves the cell.




## Won't Microorganisms Develop Resistance to Copper?

As bacteria evolve resistance mechanisms to antibiotics, might resistance to copper develop? This is highly unlikely for three reasons:

- 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.

- Copper kills microorganisms by multiple pathways rather than by acting in a specific way on one receptor like most antibiotics.

- Microorganisms are killed before they can replicate, thus they cannot pass on genetic material that could ultimately lead to the development of resistance.

## Horizontal Gene Transfer

Horizontal gene transfer (HGT) is any process in which an organism gets genetic material from another organism without being the offspring of that organism. In the case of bacteria, the exchange of genetic information occurs by passing plasmids between cells though pili, the hair-like extensions on the cell surface. Such transfers can take place between bacteria of the same or different species. When a plasmid containing DNA coding for antibiotic resistance is transferred from one bacterial species to another, a new antibiotic-resistant bacterium is created, a so-called 'superbug'.

It has been demonstrated in the laboratory that, while HGT transfers antibiotic resistance between two species of bacteria on a stainless steel surface, this does not occur on copper. The researcher explains that rapid destruction of plasmid and genomic DNA occurs on copper thus preventing the possibility of HGT.

## How Hospitals are Using Copper to Improve Infection Prevention and Control

Infection control professionals review scientific literature to keep abreast of developments and some believe there is now sufficient evidence to use copper to fight HCAIs in their hospitals. Others await further trials or official recommendations in infection control guidelines (these are starting to emerge in other countries e.g. Finland). This is a relatively new field of research – not just on copper but on the whole concept of the role of the environment in the transfer of infection.

Those installing copper have started to replace items such as door handles, bed rails, light switches, over-bed tables and taps with copper and copper alloy (brass, bronze) items to help limit pathogens and prevent their transfer around the hospital and to susceptible patients. These are some of the high-risk surfaces identified where contamination occurs and staff, patients and visitors touch.

*An installation of antimicrobial copper touch surfaces at The Bostonian Sleep Clinic in the UK. (Courtesy of Brass Age.)*

# Questions

1. **In the US trial, which surface was identified as the most heavily contaminated and how many cfu/100 cm² were there?**

2. **"Log reduction" is a mathematical term used to show the relative number of live microbes eliminated from a surface by disinfecting or cleaning. For example, 2 log reduction means the number of germs is 100 ($10^2$) times smaller.**

   **In the graph showing reduced inoculum efficacy, estimate the log reduction for the coupon with an MRSA concentration of $10^3$ CFU at 15 minutes?**

3. **Schmidt's research group reported the risk of acquiring an infection increases with the level of bacteria. What is the level of bacteria proposed as benign?**

4. **In your own school or college, make an assessment of the touch surfaces and come up with the top five high-risk list of those likely to be the most heavily contaminated with pathogens and the most frequently touched.**

Click here for answers