Potential of copper alloys to kill bacteria and reduce hospital infection rates

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Abstract

A large body of peer-reviewed literature has demonstrated in laboratory testing that placing bacteria in a highly concentrated bacterial inoculum onto copper alloy surfaces results in their rapid death. A smaller but convincing number of studies indicate that bacteria die on the surfaces of hospital room components made from copper alloys. Will the ability of copper alloys to kill bacteria translate into an ability to reduce the rate of hospital-acquired infections (HAIs)? This review addresses this question. In particular, the results of a clinical trial in which HAI rates are significantly reduced after introducing copper alloys components into Intensive Care Units of three hospitals will be presented. The findings suggest that copper alloys enhance hospital hygiene protocols because they act passively 24/7/365 requiring neither training nor human intervention to kill bacteria and reduce hospital-acquired infections.

Keywords: Antimicrobial copper alloys, hospital-infections (HAIs), clinical trial, bacterial burden, infection rates, VRE, MRSA, contact killing

Introduction

Hospital-acquired infections (HAIs), or those infections the patient develops while in the hospital, continue to be a concern because they are not only costly to treat, but more importantly, cause human suffering and even death. It was reported that, in 2002, 1.7 million patients develop an infection while being cared for in U.S. hospitals and about 99,000 die each year (1). Annual treatment cost alone for these infections is estimated to be in the range of $35 billion (2). This translates into approximately 4,600 infections resulting in about 274 deaths each day. In spite of extensive efforts to increase hand-washing compliance – an obvious, very simple, and important method to help reduce transmission of bacteria – has not been sufficient on its own to solve the infection problem.

Surface disinfectants are another widely employed and useful method to help reduce the amount of bacterial on environmental surfaces. Evidence that contaminated surfaces can function as transmission vectors for hospital pathogens is clear and control of surface contaminants should be an effective approach to controlling HAIs (3). Hygiene standards for surface cleanliness, based upon food processing industry standards, have been proposed (4). However, even when improved hand washing compliance and diligent surface hygiene disinfection are combined, hospital infections are still a serious health issue. Newer technologies, such as UV light units (5, 6) and various hydrogen peroxide (HP) systems (6), can effectively decontaminate hospital rooms, but, when added the hand washing and surface disinfection, HAIs are still not completely controlled. All the above approaches – hand washing, surface disinfection, UV light and HP systems – have one thing in common, they are episodic or one-time approaches. Therefore, as soon as the decontamination process ends, microbial contaminants can again begin to accumulate. Adding an additional technology that is continuously active – antimicrobial copper alloys – can alleviate this problem. Placing surfaces made from 100% antimicrobial copper alloys will provide a continuously active solid surface that kills bacteria on contact and thus has the potential to reduce infections. Here we review the clinical evidence supporting this potential.

Laboratory Research

A multitude of laboratory studies have shown that a wide variety of bacteria, both Gram-positive and Gram-negative, are killed after being placed on copper alloys surfaces, including "hospital superbugs" such as Methicillin-Resistant *Staphylococcus aureus* (MRSA) and Vancomycin-Resistant *Enterococcus* (VRE). Many of these studies have been summarized in previously published reviews (7, 8). Also described elsewhere is the metallurgy of various antimicrobial copper alloys and their postulated killing mechanisms (8). These studies indicate that copper alloy surfaces act as an effective biocide not only on a broad range of bacteria but also are active against fungi and permanently inactivate viruses. Table 1 lists the microorganisms that have shown sensitivity to copper alloy surface contact killing.

Clearly, copper alloy surfaces have the potential to be useful in controlling a wide variety of microbes in the hospital setting but this needs to be confirmed in clinical trials. Laboratory tests are conducted under ideal controlled conditions. The surfaces of the test samples are sanitized prior to being inoculated with a known concentration of a known strain of bacteria. In contrast, clinical samples are

collected in hospitals by taking swabs from the surfaces of components. One does not know when the surface became contaminated and the hospital surface is typical contaminated with several different species of bacteria. The surfaces analyzed in a clinical test may also contain residues from prior cleaning solutions, oil from the hands after being touched, and other chemical contaminants. Also noteworthy is that, in laboratory test conditions, the bacterial inoculum concentration is typically very high, on the order of 10 million colony-forming units per sq. cm. (10^7 CFU/cm^2). When the surface of a hospital component is sampled, swabs are usually taken from 100 cm^2 area and bacterial contamination ranges from 1,000 to 10,000 CFU/ 100 cm^2, depending on when the surface was cleaned or the frequency at which the surface is touched.

As explained above, laboratory tests are conducted by inoculating samples with an exceedingly high numbers of bacteria, well above the amount that would ordinarily be found on surfaces in hospitals. The demonstrated ability of copper alloys to kill these high numbers of bacteria in laboratory tests is a strong testament to their efficacy and bodes well for hospital-based studies. Nonetheless, antimicrobial copper alloys need to undergo testing in the real life clinical environment.

Clinical Results – microbial reduction

Microbial burden is not only a surrogate measure of cleanliness. It is also is an indicator of the propensity to acquire an infection, as will be discussed in a later section. A clinical study conducted in a medical intensive care unit (MICU) in the United States (9) measured the amount of bacteria present on 36 standard plastic patient bed rails immediately before cleaning and at set time intervals of 0.5, 2.5, 4.5, and 6.5 hours after cleaning with either of two hospital-approved disinfectants. The bacterial burden rebounded 30% at 6.5 hours after using one type of disinfectant and 45% at 2.5 hours after using another disinfectant. Thus, cleaning helps reduce bacterial burden, but its benefit is dissipated in a matter of hours.

In a subsequent study in the same hospital setting (10), three beds were custom fitted with copper alloy surface caps to cover the bed rails, with three standard plastic beds serving as control surfaces. The sampling schedule was the same as described in the previous study (9), but in contrast to the previous study, only one hospital-approved disinfectant was used. The bacterial burdens found on the copper rails were significantly lower than those measured on the standard plastic bed rails, as shown in Figure 1. Note that the copper rail bacterial burden approaches the suggested "terminal cleaning" target of 250 CFU/100 cm^2, which is the cleaning goal after a room is vacated but prior to introducing the next patient.

In the United States (11), another small trial was conducted in an outpatient infectious disease clinic. In this environment, surfaces are touched by many patients and rapidly become contaminated. Copper alloys were installed on two phlebotomy chairs. The tops of the wooden arms of the chairs were inlaid with a wide copper alloy strip, but the wood remained on the sides of the arms. In addition, the plastic trays attached to the chair arms were replaced with copper alloy trays. Over 15 weeks, 437 patients used the chairs. Results were compared to the control surfaces, the wooden arms and plastic trays on the chairs in adjacent rooms. Cleaning frequency and methods were the same. The copper tray chairs showed an 88% reduction in bacterial burden and the copper alloy inlaid arm showed a 90% reduction compared to the standard surfaces or controls. Even the

remaining wood at the side of the copper alloy inlaid chair arm displayed a 70% reduction, which was attributed to lower rate of cross contamination from the copper alloy surface. Fewer bacteria survived on the copper alloy surface and therefore a smaller number of bacteria were available to be transferred to the adjacent wood on the side of the arm of the chair.

A study (12) involving stethoscopes was conducted in the United States at two sites, a pediatric emergency division and various adult medical/surgical settings including intensive care units. Copper alloy equivalents of commercial cardiology stethoscopes were fabricated. Specifically, the diaphragm, ear tubes braiding over the polyvinyl chloride tubing, and chest piece, were replaced with copper alloys. The same parts of the commercial stethoscopes served as controls. The study, which utilized 32 stethoscopes, involved 21 healthcare providers, specifically 14 in the pediatric setting and 7 in the adult setting. They were not informed of the antimicrobial properties of copper alloys and were blinded with regard to the purpose of the trial. The study team provided either control or copper stethoscopes to the healthcare workers on an alternate basis. The devices were collected after one week of use on four occasions over 90 days, and colony counts were measured. In the adult setting, where only the copper and epoxy standard control diaphragms were evaluate, the microbial burden on the copper stethoscopes was 5 CFU/cm^2 versus 10 CFU/cm^2 on the controls, and the results were significant ($p=0.0051$). In the pediatric setting, the burden on the copper stethoscopes was 4 CFU/cm^2 versus 16 CFU/cm^2 on the controls, but the results failed to reach significance ($p=0.089$), presumably because the sample size was too small. Multiple surfaces were also sampled in the pediatric setting: the diaphragm, the ear tubes, and the braiding over the polyvinyl chloride tubing. The braiding over the chest piece was not sampled because of its irregular shape and surface area. In the pediatric setting, the aerobic colony counts recovered from the copper alloy surfaces were 11.7 CFU/cm^2, an order of magnitude lower than that found on the control surfaces, at 127.1 CFU/cm^2, and achieved strong statistical significance ($p<0.00001$).

In a clinical trial conducted in a hospital medical ward in England (13), three copper alloy components were installed: sink faucet handles, door push plates at the ward entrance, and toilet seats. Each of these surfaces was sampled once each week at 7 am and 5 pm over a ten-week period, as were equivalent non-copper control items in the ward. After five weeks the components were interchanged. The median bacterial burden reduction on the copper components compared to the control components ranged from 90% to 100%.

In a second larger clinical trial conducted in the medical ward of the same hospital in England mentioned above (14), several frequently touched components made from copper alloys were installed including door handles and push plates, grab rails, light switches and pull cord toggle switches, over-the-patient bed tables, dressing trolleys, as well as portable commodes, sink taps and fittings, sinks, toilet seats and flush handles. The above copper components and the controls were sampled once a week for 24 weeks, with the locations of the components being switched after 12 weeks. The microbial burden on 8 of the 14 copper alloy components was significantly lower than those found on the standard control components. While the other 6 copper alloy components also exhibited a reduction in bacterial burden, it was found not to be statistically significant. However, indicator organisms recovered from all surfaces provide some additional

insights. The surfaces of copper alloy components harbored significantly fewer VRE, MRSA and coliform bacteria, compared to the control surfaces.

A clinical trial was conducted in a hospital in Germany (15), in patient rooms, rest rooms, and staff rooms, and in oncology, respiratory treatment, and geriatric wards of a hospital. A total of 48 aluminum door push plates were replaced with copper alloy plates. An equal number aluminum doorknobs and plastic light switches were also replaced with components made from copper alloys. During 16 weeks in the summer and 16 weeks in the winter, samples were taken from the copper alloy surfaces and control surfaces. The total bacterial burden on the copper alloy components was 63% of that found on the control components. The total bacterial burden on copper alloy doorknobs was much lower than that found aluminum doorknobs. The bacterial burden on the both the copper alloy push plates and light switches was only slightly lower than that found on the controls made of aluminum or plastic. In addition the bacterial burden seen on the aluminum doorknobs, while higher than that found on the copper doorknobs, was also much higher than seen on the other control components. It was suggested that this difference may be simply because that doorknobs are more frequently touched relative to the other components. While the results of this trial did not achieve the same high levels of microbial burden reduction observed in other trials, the impact of the presence of antimicrobial copper alloys is apparent.

A clinical trial conducted in a Pediatric ICU in Chile involved 8 room with copper components and 8 control rooms with standard components (16). The copper surfaces included in the study were bed rails, bed rail levers, IV poles, faucet handles, and a workstation surface. The results indicated that copper alloys efficacy was equivalent to that observed in an adult ICU (17). The copper bed rail, the most frequently touched object in the rooms, showed the greatest bacterial burden. Interestingly, it was reported that the introduction of copper alloys in the study rooms suppressed the microbial burden recovered from components in the nearby control rooms, collected prior to the introduction of the copper components. It is suggested that this may be a result of suppressed cross contamination.

Another clinical trial in the United States was conducted in the medical-surgical suite in a small rural hospital (18). Six of the 13 single rooms were converted to copper, as were three of the five double rooms. The installed copper alloy components included door levers, alcohol gel dispenser push plates, light switches, bedside table pulls, over-bed tables, toilet flush valve lever, grab bars, faucet handles, and soap dispenser push plates. Copper alloy beds were not fabricated, but a commercial copper alloy stretcher bed, used for patient transport by the emergency department, was included in the trial. The mean bacterial burden recovered from the copper alloy components was 140 CFU/100 cm^2, which is well below the 8,414 CFU/100 cm^2 found on the controls and slightly below the terminal cleaning target level of 250 CFU/100 cm^2.

A large clinical trial was conducted in the Unites States in the ICUs of three hospitals over 43-month period (17). At month 23, six copper components were installed in eight of the sixteen ICU rooms. The components were the rail of the patient bed, the nurses call button, the arms of the visitor's chair, the over-the-patient bed table, the intravenous (IV) drip pole, and a data input device that varied by hospital. The latter was either a computer mouse, the bezel on a touch screen, or a strip where the

palm of the hand rests on a laptop computer. Microbial burden was measured on the six copper components and six standards components that served as controls over the next 21 months. The data collected from the six objects is presented in Figure 2. Note that the control bed rail has the highest level of microbial burden, but this is dramatically lower on the copper bed rail. The bed rail is the major point of interaction between patients, healthcare workers and visitors, which may explain the high microbial burden on the plastic bed rail. The controls for the nurses call button and arms of the visitor's chair also had high levels of contamination. However, the bacterial burden on all the copper components were below that seen on the standard or control surfaces, except for the data input devices, which is an anomaly. The contamination levels of both the control and copper data input devices were both low. The use of these devised is restricted to healthcare professionals who are more aware of the potential for infections and may clean them and their hands more frequently.

Clinical Results –infection reduction

A follow-on study (19), conducted at the same facility in Chile as described previously (16), analyzed hospital-acquired infections in 261 patients in the copper rooms and 254 in the control rooms. The study found that infection rates were 10.6 per 1000 patient days in the copper room and 13.0 in the control rooms. This translated into a relative risk reduction of 0.19. These authors reported that the above result was not did not achieve statistically significance and concluded, "Conducting clinical trials to assess interventions that may impact HAI rates is very challenging."

A next phase of the previously mentioned clinical trial in the Unites States (17), also conducted in the ICUs of three hospitals, shifted its focused from microbial burden to infection rates (20). The sampling continued as previously described but the healthcare workers were not informed that that approval had be granted by the Internal Review Boards of all the involved institutions to track infections. The number of infections over the same time period in copper and control rooms were compared. Clinicians at each hospital determined incidents of hospital-acquired infections, according to National Safety Network definitions. However, the clinicians were "masked" or "blinded" with regard to the identity of patients. The infection rates were 3.4% in the copper rooms (10 infections in 294 patients) and 8.1% in the control rooms, or 26 fewer infections than in the 320 control patients. A high level of statistical significance (p value =0.013) was attained. This equates to 58% reduction in infections as a result of introducing only six copper items into each copper room, comprising less than 10% of their surface area. The data plotted in Figure 3, collected during this clinical trial, indicates that the propensity to acquire an infection increases as the microbial burden increases. Thus, infection rates correlate with surface contamination levels. The figure includes all data from both copper and control rooms, and is statistically significant, as indicated by its p value of 0.038. These results (20) can be used to calculate the cost of recovery time for outfitting a copper alloy room. The additional cost to fabricate the copper components was about $52,000. The cost to treat an infection ranges from $28,400 to $33,800 (2). The number of infections prevented in this trial is 14. Based upon the above cost per infection, the time to recover the cost of outfitting the ICU with copper components is calculated as 37 to 44 days (7).

Conclusions

There is a considerable body of literature that indicates that bacteria die when they come into contact with copper alloy surfaces in the laboratory as well as a meaningful but smaller number of publications that illustrate that copper alloys kill bacteria in the clinical setting. While additional clinical trials are needed to confirm that the deployment of solid copper alloy surfaces can reduce infection rates, there is ample evidence currently available to encourage hospitals and other patient treatment centers to adopt the use of antimicrobial copper alloys as part of their infection control protocols.

The copper alloy components used in the studies referenced here were fabricated from 100% solid metal. The copper alloys used must contain at least 60% copper to be considered for EPA registration, which is required in make public health claims in the United States related to their ability to kill specific bacteria. The copper alloy was not applied as a coating, which can wear off, or introduced as particles in proprietary plastic matrix that make up less than 5% of the surface area.

The initial cost of outfitting a copper alloy room may be perceived as an issue. However, the extra cost can be quickly recovered because infections are expensive to treat. Based upon the number of infections prevented in ICUs of three hospitals (20), the extra cost of copper components was recaptured in less than two months (7). It should also be noted that some hospitals would loose a portion of their Medicare funding under the Hospital Acquired Condition Reduction Program (21) if hospital-acquired infections occur in their facilities. It is important to note that there is no identified medical risk in using antimicrobial copper alloy hospital room components. Humans have commonly used copper alloys since the Bronze Age, over 5 millennia ago, without any evidence of harm. Clearly, placing copper alloy components in the human environment has the potential to reduce infections, may avoid the above-mentioned financial penalty, and will lower infection treatment costs. Antimicrobial copper alloys may also have intangible benefits, such as, demonstrating to your patients that your organization cares about their wellbeing.

Perhaps the greatest potential benefit of wider use of antimicrobial copper alloys to control infection has the potential to inhibit the emergence of new antibiotic resistant strains. Based on reports from the U.S. Center for Disease Control, the abuse and overuse of antibiotics is a major cause of the emergence of resistant bacteria (http://www.cdc.gov/drugresistance/). The use of subclinical levels of antibiotics in raising animals for human consumption is a serious contributor to this problem (22). Also to be considered is that horizontal gene transfer of antibiotic resistance, a major cause of the spread of multidrug resistance in bacteria, is essentially blocked by copper alloy surface killing because the bacteria die rapidly with few to no survivors (23).

Nearly 200 facilities have installed antimicrobial copper products provided by U.S. based EPA registered manufacturers, in 37 states and 13 countries. These installations include healthcare facilities, schools and universities, office buildings, fitness facilities, laboratories and restaurants. Copper alloys are a passive antimicrobial technology that works 24 hours/day, 7 days/week, and 365 days/year. Its effectiveness in killing bacteria and potentially reducing infections requires neither specially trained personnel nor human intervention. A wide array of commercial products made from EPA-registered antimicrobial copper alloys is available for integration into the healthcare environment.

In summary, consideration should be given to deploy components made from solid metal antimicrobial copper alloys as an additional tool in the fight to reduce hospital-acquired infections.

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Conflict of Interest
The authors have no conflict of interest directly relevant to this manuscript.

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Table 1. Microorganisms that are known to die on copper alloy surfaces (taken from (8))

Microorganism	**Reference**
Bacterial species	
Acinetobacter species (MDR, other strains)	(24), (25), (26), (27)
Bacillus anthrax, B. cereus, B. subtilis (vegetative cells, not spores)	(28), (29), (30)
Brachybacterium conglomernatum	(27)
Brucella melitensis	(29)
Burkholderia species	(29), (31), (32)
Campylobacter jejuni	(33)
Clostridium difficile (vegetative cells, not spores)	(34), (35)
Deinococcus radiodurans	(28)
Enterobacter species	(25), (36), (37)
Enterococci species (vancomycin – resistant, other strains)	(38), (39), (40), (41), (42)
Escherichia coli (various strains)	(28), (38), (43), (44), (45)
Francisella tularensis	(29)
Klebsiella pneumonia	(23), (24), (25)
Legionella pneumophila	(46), (47), (48), (49)
Listeria monocytogenes	(50), (51)
Mycobacterium tuberculosis	(24)
Pantoea stewartii	(27)
Pseudomonas species	(25), (26), (27), (36), (38), (41)
Salmonella enterica	(33), (39), (52)
Staphylococcus aureus (MRSA, other strains); other *Stapyloccoccus* species	(26), (27), (38), (53), (54), (55)
Yersinia pestis	(29)
Viruses	
Coronavirus 229E (human)	(56)
Influenza A	(57)
Norovirus (murine, human)	(40), (58), (59)
T2 bacteriophage	(60)
Vaccinia, Monkeypox	(29)
Fungi	
Aspergillus species	(46)
Candida albicans	(24), (46), (61)
Fusarium species	(46)
Penicillium chrysogenum	(46)
Saccharomyces cerevisiae	(61)

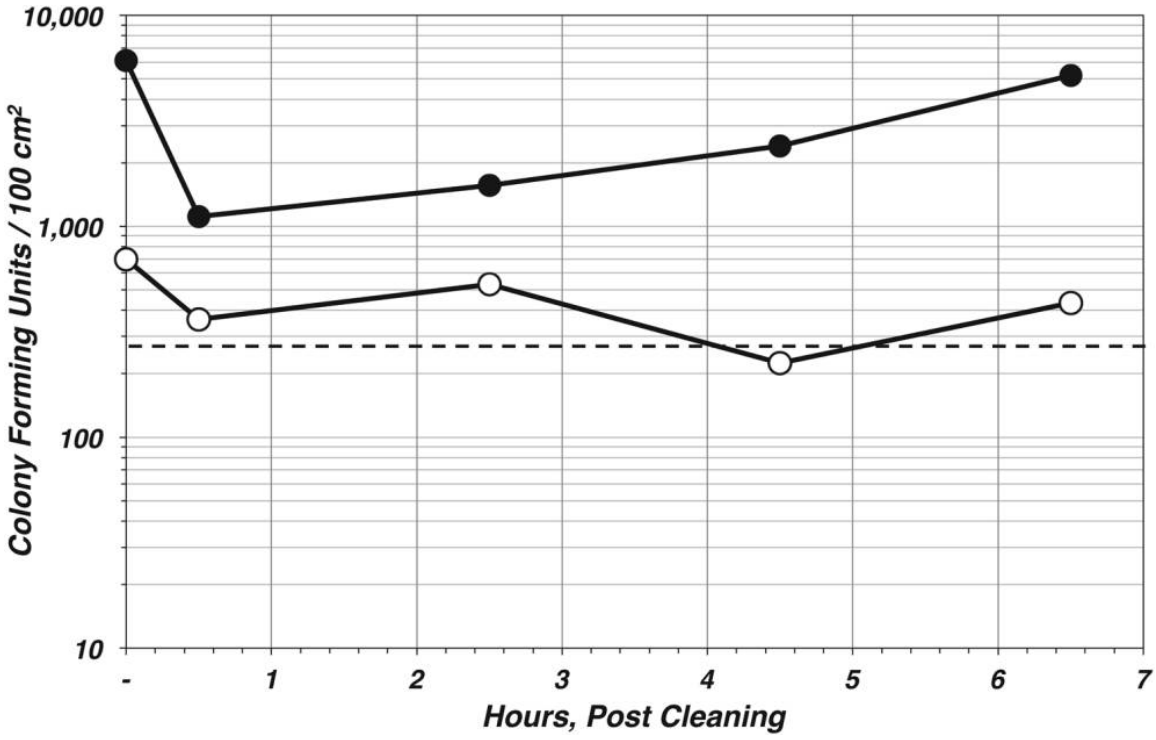

Figure 1: Microbial burden found on the standard plastic rail (filled circles) and copper rail (open circles). The dashed line is the desired target microbial burden after terminal cleaning of 250 CFU/100 cm^2 (taken from (10)).

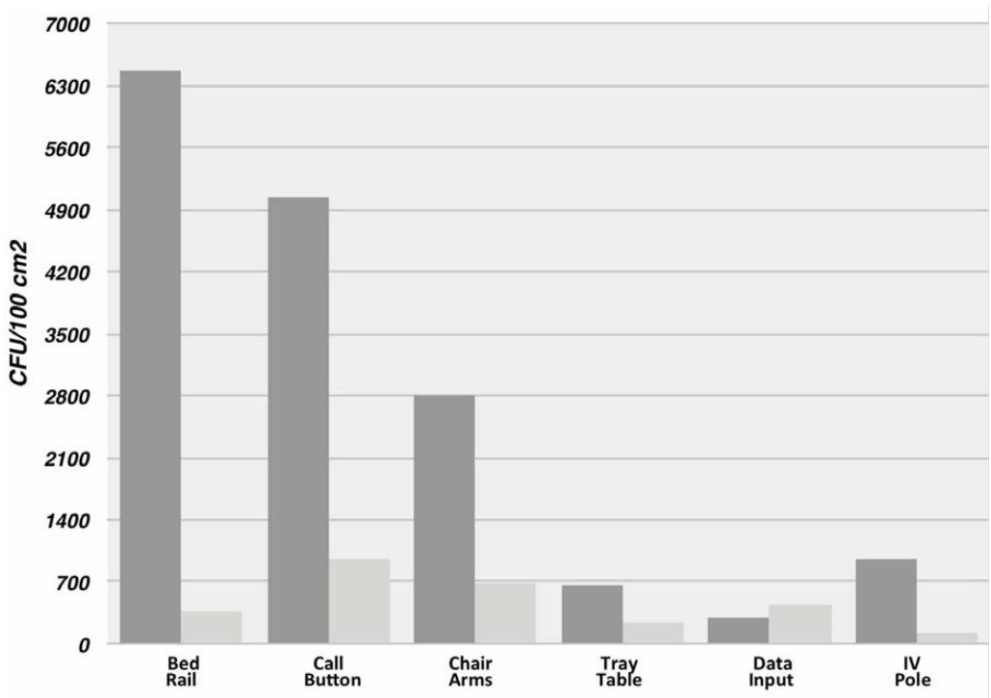

Figure 2: Microbial burden found on six objects in standard control rooms (dark gray bars) and copper rooms (light gray bars) in hospital intensive care units (ICUs) (taken from (17)).

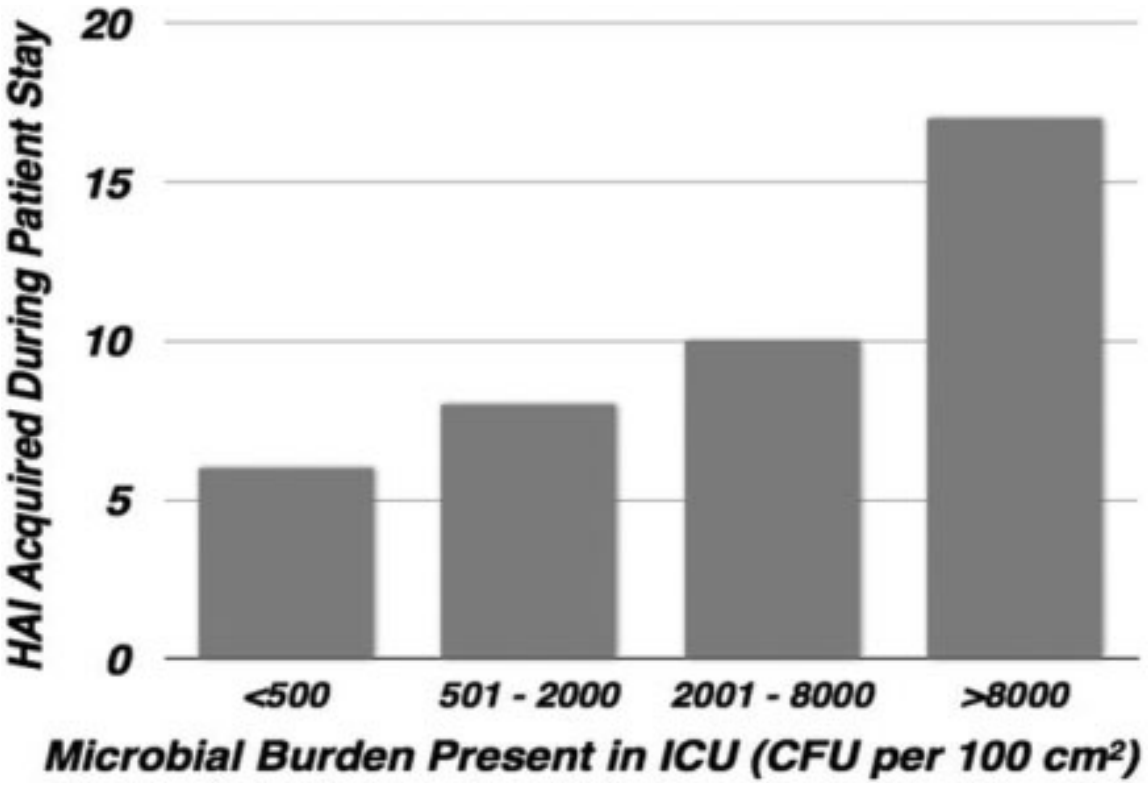

Figure 3. Relationship between microbial burden measured in ICU rooms and the occurrences of hospital-acquired infects (HAIs) (taken from (20)).

