Self-disinfecting and Microbiocide-Impregnated Surfaces and Fabrics: What Potential in Interrupting the Spread of Healthcare-Associated Infection?

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Innovative technologies have identified approaches to developing self-disinfecting surfaces or fabrics to minimize healthcare-associated infection (HCAI). These include altering the structure or surface to minimize the attachment of microbes or to delay the development of biofilm, using compounds that are activated in the presence of light to reduce the microbial burden, and incorporating a heavy metal such as silver or copper with intrinsic antimicrobial activity. Most technologies for surfaces and fabrics have been assessed in vitro and have been shown to reduce bacterial numbers by ≥2 logs. However, apart from copper-impregnated surfaces, there have been few trials in a clinical setting. Copper-impregnated surfaces result in reduced microbial surface counts on surfaces commonly found in clinical areas compared with controls, and 1 study has assessed HCAI and colonization rates. However, larger and better-designed studies are required to determine if these approaches augment current hygiene regimens, especially when these are optimally implemented.

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Recent years have seen a welcome reassessment of the role of the inanimate environment in the epidemiology of healthcare-associated infection (HCAI). While most infections are multifactorial, substandard hospital hygiene has been implicated in a number of outbreaks and incidents. For example, as recently reviewed, there is increasing evidence of the likelihood of a single-room occupant acquiring a nosocomial pathogen if the previous occupant was also positive for the same pathogen [1]. Many bacteria, especially staphylococci and Acinetobacter, can survive for considerable periods of time in the environment, and methicillin-resistant Staphylococcus aureus (MRSA) can be detected in the immediate vicinity of colonized patients as well as in the air, with the potential for localized spread [2]. Moreover, this often occurs in the setting of suboptimal hygiene practice. In a study of intensive care units, just under 50% of surfaces were cleaned adequately and the thoroughness of cleaning did not correlate with hospital size, case mix, or geographic location [3]. After feedback delivered through the use of fluorescent stains visible on ultraviolet light, cleaning improved to 82%.

Environmental decontamination involves the use of water, detergents, and, increasingly, a disinfectant or microbiocide, but the effectiveness of any agent is dependent on how well it is applied and the rigor with which cleaning/decontamination is undertaken. However, there is no consensus on assessing hygiene from a microbiological perspective, and this has hampered studies in this field. The relationship between what may be found in the environment and the risk of acquisition by a patient is complex and not just related to how many of the bacteria acquired by the patient were present in the immediate environment. The use of standards from the food industry to assess hospital hygiene has been...
suggested; for example, on hand touch surfaces there should be <5 colony-forming units (CFU)/cm² and <1 CFU/cm² for indicator organisms such as MRSA [4]. There is also an awareness of the potential for microbiocide resistance to emerge and the wider environmental implications of more microbiocides being discharged from hospitals [5]. There is a range of novel technologies available or being developed in the healthcare sector and in others, for example, the agri-food sector, that may have a role including microbiocide-impregnated surfaces or fabrics. Page and colleagues have reviewed the different approaches and the scientific basis behind the technology, which include various coatings and alterations in surfaces such as light-activated antimicrobial agents [6]. What follows is a review of the current technology and its potential application specific to the healthcare setting.

SELF-DISINFECTING OPTIONS

In developing a self-disinfecting surface, it is important not to fundamentally alter the components of that surface or fabric, such that it remains capable of doing what it was designed to do, for example, in the case of a surface to be durable and in the case of a fabric to be comfortable to wear and to be washable. To date, current approaches have been:

- Altering the surface components to minimize the likelihood that bacteria will adhere or replicate;
- Coating the surface or fabric with an acknowledged antimicrobial compound whose activity persists;
- Using a material that has some inherent antibiofilm or microbicidal activity.

The need for effective decontamination and to maintain surfaces relatively microbe-free is also necessary in other areas. Banerjee and colleagues have reviewed some of the coatings used in marine settings to minimize fouling [7]. These include enzymes, photoactive materials, and self-assembled monolayers. For example, polyethylene glycol (PEG) confers protein resistance to a surface but may auto-oxidise over time, thus losing its activity. Most bacteria causing infection exist in biofilms, complex structures through which microbiocides may have difficulty penetrating. Consequently, preventing the development of biofilm on a surface reduces microbial buildup and assists the cleaning process. If a surface is in contact with stagnant fluids when biofilm is more likely, altering the surface topography through surface nanostructuring or coating with antimicrobial compounds (eg, silver) are potential approaches to minimizing or delaying biofilm formation [8]. Although bacteria vary in their capacity to form biofilm, the immediate environment has a significant influence; for example, heparin significantly enhances the formation of biofilm in vitro compared with saline on a polyvinyl fluoride surface [8]. Another factor is the charge buildup on surfaces that may impact on the settling of bacteria. The use of negative air ionizers alters the electrostatic balance of surfaces in the clinical environment, resulting in some bacteria (eg, Acinetobacter species) being repelled from surfaces [9].

Photoactivated Surfaces

A well-described approach to maintaining surfaces relatively microbe free is to coat the surface with a photoactivated self-cleaning film. The most commonly used photoactive material is titanium dioxide (TiO₂). When ultraviolet light comes in contact with the photosensitive surface, active oxygen species are released following the relaxation of electrons to the ground state from the excited singlet state, resulting in an antimicrobial effect due to the emission of light. Reactive oxygen species include superoxide and hydrogen radicals, which have antimicrobial properties [7]. Titanium dioxide has been used in a number of materials, including plastics and in healthcare items such as surgical face masks [10]. Scanning electron microscopy reveals the extent of damage to the cell wall, and death occurs when there is irreversible leakage of intracellular molecules. Similarly, TiO₂ glass plates were shown to inactivate RNAse and lipopolysaccharide, important markers of contamination in the pharmaceutical industry [11].

The use of other photosensitizers, such as toluidine blue O and rose bengal, has been shown to reduce bacterial counts underneath a suspended lamp in a UK dental clinic, and the surviving bacteria were low-grade commensals such as Micrococcus luteus [12]. However, the authors acknowledge that the clinical environment may be challenging both in terms of providing a constant source of photoactivation, and because of the variation in temperatures commonly encountered. In a more recent study from the same group in the United Kingdom, the incorporation of gold nanoparticles and methylene blue in silicone polymers resulted in a greater reduction in surface counts of aerobic and anaerobic bacteria, compared to surfaces with methylene blue only [13].

Other Approaches

Many bacteria secrete lytic enzymes to gain a competitive advantage in their natural environment and which target the cell wall of other bacteria. Pangule and colleagues have developed nanocomposites containing different conjugate formulations with enzymes highly effective against MRSA [14]. The authors suggest this approach in the development of different antimicrobial paints with different enzymes resulting in reduced surface counts. However, it is unclear if the activity persists over the normal period of time that occurs in between the routine painting of surfaces.

Another approach to delaying biofilm formation has been to mimic the skin of a shark through microtopography to include rectangular ribs of 2–3 μm in a diamond-like array that in nature
inhibits the attachment of barnacles [15]. This has been shown to significantly delay but not completely prevent biofilm formation as analyzed by scanning electron microscopy for ≥7 days. Cheng and colleagues have attempted to use hydrophilic polymers such as PEG on surfaces and have successfully reduced the adherence of both *Staphylococcus epidermidis* and *Pseudomonas aeruginosa* as assessed by fluorescent microscopy on contaminated surfaces [16].

**IMPREGNATED FABRICS**

Some of the above-described principles can be utilized to minimize the adherence or replication of bacteria on fabrics and thus reduce the likelihood that the clothes or personal attire of healthcare workers will spread infection from patient to patient. However, the antimicrobial effect should not change function; that is, fabrics must remain durable and impenetrable to fluids, and for nondisposable items, can be successfully rewashed without loss of antimicrobial effect.

Woven and nonwoven fabrics coated with hydroxyapatite-binding silver TiO₂ were assessed in an in vitro study. Bacterial counts on woven and nonwoven fabrics decreased by approximately log₂, but counts decreased more rapidly on nonwoven fabrics [17]. Chitosan is nontoxic and biodegradable, and at varying concentrations, its incorporation into cotton fabric reduced the numbers of staphylococci by log₆, resulting in the authors’ advocating this in reducing exacerbations of skin conditions such as atopic dermatitis, which may be precipitated by staphylococci and other bacteria [18].

A commercially available textile, with and without the incorporation of silver (ie, Cliniweave), was shown to have significant antibacterial activity with a log₂₃ reduction of *S. aureus* after 60 minutes during an in vitro study [19]. However, the authors acknowledge the necessity for clinical trials to determine its effectiveness and applicability. In a veterinary medicine clinic, silver-impregnated surgical scrub tops compared with polyester/cotton scrubs had significantly fewer bacteria at both 24 and 48 hours but not at 4 and 8 hours; the lumbar area was associated with higher bacterial counts, as were circumstances in which animals had to be restrained [20]. This indicates that silver takes a number of hours to reduce bacterial counts on fabrics compared with nonimpregnated fabrics, but its potential impact in both protecting staff from work-associated infections or in reducing cross-transmission needs to be further assessed.

Another approach has been the incorporation of a quaternary ammonium salt that inhibits bacteria and fungi and which can be incorporated onto surfaces and into patient gowns. Using a methodology developed by the American Association of Textile Chemists and Colorists, swatches of control and test fabrics were inoculated with bacteria kept at room temperature and then exposed to air for 14 days [21]. There was a more rapid decay in the numbers of MRSA, *P. aeruginosa*, and *Escherichia coli* on treated compared with untreated fabrics over a period of up to 14 days.

Fabrics containing 20% copper were assessed for their antimicrobial effect to offset the potentially irritating effects of microbes precipitating some skin disorders [22]. Copper-impregnated fabrics led to a log₆ reduction in *E. coli* and *S. aureus* within 2 hours. There was also activity against dermatophytes and yeasts such as *Candida albicans*. The products did not have skin-irritating properties as determined by animal model assessments, and they retained activity against *S. aureus* after 35 washes at 85°C [22].

**HEAVY METAL–IMPREGNATED SURFACES**

Heavy metals have antimicrobial properties and this has been used to characterize microorganisms using an extended resistogram with antibiotics. Silver has also been incorporated into medical devices such as central venous catheters to reduce infections. This principle has been applied to surfaces.

**Silver**

Citrate-capped/nanosilver particles were assessed for their antimicrobial activity against *S. aureus* and *P. aeruginosa* in both planktonic and sessile forms on titanium [23]. There was a significant reduction in counts for both organisms, but greater for *P. aeruginosa*, possibly due to the different cell structure between gram-negative and -positive bacteria. Bright and colleagues evaluated a stainless steel surface coated with silver and zinc. These metals were incorporated into zeolite ceramic coatings, which are composed of gridlike structures forming porous crystals, in which the ions reside. There was a significant falloff in numbers of *S. aureus* after 4 hours by log₂, which was greatest at 24 hours [24]. However, it is not clear from this study whether there would be residual activity beyond 24 hours.

Using flame-assisted chemical vapor deposition of a coating containing silver and silica, activity was assessed on glass and ceramic tiles [25]. There was a log₅ reduction in *E. coli* and *S. aureus* within 4 hours, but a similar reduction in antibiotic-resistant bacteria (eg, MRSA) took 24 hours. After 2 weeks, the coated tiles had a 95% lower surface contamination rate than controls, and although a washing cycle reduced activity, there was still a log₂ reduction in bacterial counts after 4 hours [25]. Further research is required to determine if antimicrobial activity persists for prolonged periods of time (ie, months and years), and what impact repeated cleaning/washing of the surface has on activity.

**Copper**

The use of copper for its antimicrobial activity dates back to ancient Egypt [26, 27]. The cause of bacterial cell death due to exposure to copper may relate to its ability to accept and donate...
single electrons leading to the generation of reactive oxygen species, resulting in cell lysis [26]. Most approaches to date have been to incorporate copper into commonly touched surfaces such as door handles, toilet seats, etc. There is considerable variation in the constituents of copper alloys that may be used; the higher the copper concentration, the greater the antimicrobial activity. Copper has activity against a range of bacteria, including spore-forming bacteria such as Clostridium difficile, MRSA, and both yeasts and molds (eg, Aspergillus fumigatus) [28–30].

The use of copper-impregnated surfaces has also been the subject of discussion in the food industry; it has been shown to have excellent activity against E. coli O157, an important cause of food poisoning with up to a 7-log kill after 90 minutes for alloys with ≥99% copper content [31]. However, issues about durability and its susceptibility to corrosion in this setting limit the use of copper-impregnated surfaces. As with any microbiocide-impregnated surface, there are questions to be answered about activity over time after soiling and repeated cleaning and the potential emergence of copper resistance among bacteria. Airey and Verran found that after repeated soiling over 2–5 days, there was a significant buildup of cell mass, but with stainless steel having a lower level of soil compared with copper [32]. Of 62 hospital environmental isolates of Enterobacteriaceae recovered from 428 surfaces in 3 hospitals over 4 months, all were resistant to copper [33]. Santo and colleagues evaluated the factors affecting copper resistance using copper-containing metallic coins [34]. A diverse collection of bacteria were studied, and bacteria, especially gram-positive bacteria were more resistant to the activity of dry than moist copper surfaces [34]. This suggests a complex interaction between different bacteria, antibiotic-resistant mechanisms among the exposed bacteria, and the nature of the interaction with copper that requires further study.

Although it is clear that copper impregnated onto surfaces has antimicrobial properties and potential as an intervention to prevent and control HCAI, it is only in the last few years that there have been studies applying this in clinical settings. Karpanen and colleagues undertook a crossover study in an acute care medical ward in the United Kingdom where 14 frequently touched copper-impregnated items (content varying from 60% to 99% copper) were installed and microbial counts and the presence of indicator organisms were assessed [35, 36]. While the study does provide details of the routine cleaning regimen, there was no assessment of the effectiveness of routine cleaning over the study period. Nonetheless, neither staffing levels, compliance with hand hygiene, or bed occupancy varied significantly between the control and intervention periods. However, 8 of the 14 items demonstrated significantly lower bacterial counts compared with standard materials, and there were significantly lower numbers of vancomycin-resistant enterococci (VRE), methicillin-susceptible S. aureus, and coliforms recovered from the copper-impregnated surfaces. None of the isolates tested, which included MRSA, VRE and coliforms, were reported as resistant to copper, but ongoing surveillance would be required to confirm that over a prolonged period of time.

In a 6-month study carried out in a consulting room in South Africa, there was a 71% reduction in the mean bacterial colony counts on the copper-impregnated surfaces (copper content 99%) compared with controls [37]. In a study carried out in 3 hospitals over a 43-month period of 6 objects installed in intensive care units (ICUs) with weekly sampling, the average microbial burden on surfaces exceeded that recommended (<250 aerobic CFU/100 cm²) by a factor of 28 during the preintervention period but fell significantly after the copper-impregnated surfaces (content varying from 60% to 99% copper) were introduced, with no MRSA or VRE being detected on these surfaces [38]. More recently, in an ICU, the bed rails in 3 ICU beds were custom-fitted with 99.9% metallic copper, and bed rail sampling was conducted over 3 months, before and up to 6.5 hours after cleaning [39]. Although there was an initial 10-fold reduction in bacterial counts on standard bed rails after cleaning, the numbers returned to the near pre-cleaning levels after 6.5 hours. In contrast, there were significantly lower numbers of bacteria on the copper-impregnated bed rails before cleaning and afterward.

Salgado and colleagues have carried out the first study to claim a reduction in HCAI/colonization rates arising from the use of copper-impregnated surfaces (content varying from 60% to 99% copper) [40]. Patient demographics, the results of environmental sampling, and outcome measures (ie, rates of HCAI and/or MRSA/VRE colonization) were monitored. Infection and/or colonization with MRSA or VRE occurred in 7.14% of patients in rooms with copper-impregnated surfaces compared with 13% in rooms without, a statistically significant difference. There was a reduced number of surface bacteria recovered from rooms with copper-impregnated objects, and the risk of acquiring an HCAI was significantly associated to the microbial burden [40]. The authors of this study suggest that copper surfaces may reduce HCAI rates; however, further studies are required to confirm this. Furthermore, some aspects of the study have been criticized, including the reporting of study outcomes, possible high interobserver variability when determining endpoints (eg, detection of MRSA and VRE acquisition), and issues about the biological plausibility of a measure to reduce HCAI when the major sources are endogenous and not exogenous bacteria—the bacteria that copper-impregnated surfaces are likely to reduce [41].

**CONCLUSIONS**

**Further Clinical Trials**
It is clear that there are many innovative and potentially exciting ideas to reduce the numbers of microbes on surfaces, and
those relating to surfaces are summarized in Table 1. Although many of these have proven microbiocidal effects, it is essential to confirm that any modifications in surfaces or fabrics do not compromise functionality ahead of what normally might be expected, and that the microbiocidal activity persists in the face of repeated soiling and washing. What is needed is collaboration between industry and infection prevention and control practitioners to design rigorous studies that will control for variables, such as patient demographics, compliance with hand hygiene, and the efficacy of environmental decontamination.

Assessments of Healthcare Hygiene

Carling has recently reviewed the various objective methods for evaluating environmental hygiene including observation, bacterial culture, fluorescent markers, and the use of rapid adenosine triphosphate bioluminescence (ATP) [42]. Bioluminescence-based ATP assays, as commonly used in the food industry, have been assessed in the healthcare environment, with some of the limitations highlighted: for example, the results vary according to the relative light unit threshold chosen to distinguish clean from contaminated, and ATP results may not always reflect bacterial counts [43–45]. Microbiological methods as part of an assessment of hospital hygiene or in research vary according to methods of sampling and the culture media used [46]. More recently, Bokulich and colleagues have assessed the use of high-throughput microbial sequencing to assess bacterial and fungal contamination on a range of surfaces in a neonatal ICU with the potential for much more rapid results compared with culture [47].

Future Role

Any new technology is unlikely to obviate the need for conventional and necessary infection prevention and control measures. Furthermore, most of the technologies evaluated to date reduce bacterial numbers by log$_{2-3}$ but do not eradicate all bacteria. However, impregnated surfaces or fabrics may be shown to have a role after further studies and be indicated where, despite the optimization of conventional approaches, infection rates remain high. It is an advantage that, once installed, these technologies require minimal expertise on the part of healthcare workers; however, studies are needed to prove that they have a role for routine use in the healthcare setting.

**Notes**

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