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Self-disinfecting surfaces: Review of current methodologies and future prospects

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Methods to improve disinfection of environmental surfaces in hospital rooms include improving cleaning/disinfection by environmental service workers through education and feedback on cleaning effectiveness (eg, use of fluorescent dyes), “no-touch” methods (eg, UV-C light), and self-disinfecting surfaces. Self-disinfecting surfaces can be created by impregnating or coating surfaces with heavy metals (eg, silver or copper), germicides (eg, triclosan), or miscellaneous methods (eg, light-activated antimicrobials). These methods are under active investigation but to date have not been assessed for their ability to reduce health care-associated infections.

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More than 20 years ago, Dr Robert Weinstein estimated that source of pathogens for health care-associated pathogens was cross infection via the hands of health care personnel (HCP) is 20% to 40% and the environment is another 20%.¹ In the intervening years, substantial scientific evidence has accumulated that contamination of environmental surfaces in hospital rooms plays an important role in the transmission of several key health care-associated pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* species (VRE), *Clostridium difficile*, *Acinetobacter* species, and norovirus.²⁻⁴ All of these pathogens have been demonstrated to persist in the environment for hours to days (and in some cases for months), to frequently contaminate the surface environment and equipment in the rooms of colonized or infected patients, to transiently colonize the hands of HCP, to be associated with patient-to-patient transmission via the hands of HCP, and to cause outbreaks in which environmental transmission was deemed to play a role. Furthermore, hospitalization in a room in which the previous patient had been colonized or infected with MRSA, VRE, *C difficile*, or *Acinetobacter* species has been shown to be a risk factor for colonization or infection with the same pathogen to the next patient admitted to the room.^{3,4}

Pathogen transfer from an infected patient to a susceptible patient occurs most commonly via the hands of HCP, but contaminated hospital surfaces, medical equipment, water, and air can be

directly or indirectly involved in the transmission pathways. These transmission pathways and methods to interrupt transmission have been diagramed.^{4,5} HCP have frequent contact with the environmental surfaces in patient's rooms, providing ample opportunity for contamination of gloves and/or hands.⁶ Furthermore, it has been observed that there is lower compliance with hand hygiene by HCP following contact with the patient's environment than directly with the patient.⁷ Hand contamination with MRSA has been demonstrated to occur with equal frequency when HCP contact a colonized/infected patient or through only touching contaminated surfaces.⁸ Finally, the most significant risk factor for hand/glove contamination of HCP with multidrug-resistant pathogens has been demonstrated to be positive environmental cultures.⁹

Potential methods of decreasing the frequency and level of contamination of environmental surfaces in hospital rooms have included routine and terminal disinfection with chemical germicides¹⁰ and, more recently, the use of “no touch” methods of terminal room disinfection with ultraviolet (UV) light or aerosolized and/or vaporized hydrogen peroxide.¹¹ Unfortunately, routine and terminal cleaning of room surfaces by environmental service workers and portable medical equipment by nursing staff is frequently inadequate. Multiple studies have demonstrated that less than 50% of hospital room surfaces are adequately cleaned and disinfected when chemical germicides are used.^{12,13} However, with implementation of enhanced performance feedback, education, and other interventions, the frequency of appropriate cleaning can be increased to 71% to 77%.^{13,14} Similarly, inadequate cleaning of portable medical equipment by nursing staff has also been demonstrated.¹⁵ The use of “no-touch” methods such as devices that emit UV light or produce hydrogen peroxide have been developed to improve room disinfection. However, a major

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limitation of these technologies is that currently they can only be used for terminal room disinfection because they require removal of the patients and HCP from the room. Other limitations include the high acquisition costs of room decontamination units and increased time of room turnover.¹¹

Recently, another method of reducing the frequency and level of surface contamination in hospital rooms has been described: self-disinfecting surfaces (Table 1). Such surfaces have also been called “self-sanitizing,” and, because microbial killing requires direct contact with the surface, the term “contact killing” has also been used. This paper will expand on our recent commentary on this subject,¹⁶ as well as providing updated information.

SURFACES IMPREGNATED OR COATED WITH A HEAVY METAL

Heavy metals comprise approximately 65 elements that are considered metals and have a specific gravity greater than 5.^{17,18} Most heavy metals are either insoluble or extremely rare, and their effects on biologic systems are of minor importance. However, more than 30 heavy metals are potentially able to interact with microorganisms including silver (Ag), gold (Au), bismuth (Bi), cobalt (Co), copper (Cu), iron (Fe), mercury (Hg), manganese (Mn), nickel (Ni), lead (Pb), platinum (Pt), antimony (Sb), tin (Sn), titanium (Ti), and zinc (Zn). It has been known since antiquity that some heavy metals possess anti-infective activity. Among the use of heavy metals to prevent or treat infections has been the use of copper-clad ships to resist the growth of barnacles; mercurials, arsenic derivatives and bismuth compounds to treat syphilis; silver nitrate to prevent gonococcal neonatal conjunctivitis, and silver compounds as topic agents to prevent infection in burn patients.¹⁷ Despite the fact that modern antibiotics have largely replaced heavy metal therapeutics for treating infection, intense research is being conducted into the use of heavy metal containing complexes (platinum, copper, zinc, and gold) for the treatment of cancer¹⁹ and metal-based drugs (antimony, ruthenium, gold, platinum, palladium, and zinc) for the treatment of malaria, trypanosomiasis, and leishmaniasis.²⁰ Although the development of self-disinfecting surfaces impregnated or coated with silver or copper is farthest advanced (see below), the use of other heavy metals such as titanium is also being studied.²¹

Silver

Silver has been used extensively throughout recorded history for a variety of medical purposes.²² Silver compounds continue to be used for topical antiseptics (eg, silver nitrate and silver sulfadiazine).²³ The effectiveness of central venous catheters impregnated with silver sulfadiazine-chlorhexidine or silver iontophoretic in preventing central line-associated bloodstream infections has been demonstrated in multiple randomized clinical trials and meta-analyses.^{24,25} Other indwelling medical devices impregnated with a silver compound have been developed including endotracheal tubes²⁶ and urinary catheters.²⁷ More recently, silver nanoparticles have been incorporated into wound dressings, indwelling catheters, bone cement and other implants, clothing and environmental surfaces and some of these products are now commercially available.²⁸⁻³⁰

Silver ions have the highest level of antimicrobial activity of all the heavy metals.³¹ Although many mechanisms for silver's bactericidal activity have been proposed, the observed bactericidal efficacy of silver is thought to be through the strong binding with disulfide (S-S) and sulfhydryl (-SH) groups found in the proteins of microbial cell walls. Through this binding event, normal metabolic processes are disrupted, leading to cell death.³¹ Both intrinsic and acquired silver resistance has been well described in bacteria.^{31,32} The major mechanisms appear to be either exclusion of silver from the bacterial cell or mobilization outside the cell.³¹

Table 1
Self-disinfecting surfaces: Possible methodologies

Methodology	Options
Surface impregnated with a metal	Silver; copper
Surface impregnated with a germicide	Triclosan; antimicrobial surfactant/quaternary ammonium salt
Miscellaneous	Altered topography; light-activated antimicrobial coating

NOTE. Adapted from Weber and Rutala.¹⁶

Silver may be added to polymers to confer antimicrobial activity and has been incorporated into such consumer products as toys, telephones, and infant pacifiers.³¹ To date, only one product (Surfacine; Surfacine Development Company, Tyngsborough, MA) has been assessed for use as a self-disinfecting surface in hospitals. It incorporates a water-soluble antimicrobial compound (silver iodide) in a surface-immobilized coating (a modified poly-hexamethylenebiguanide) that is capable of chemical recognition and interaction with the lipid bilayer of the bacterial outer cell membrane by electrostatic attraction.³³ Microorganisms contacting the coating accumulate silver until the toxicity threshold is exceeded. Surfacine can be applied to inanimate surfaces by dipping, brushing, or spraying without prior surface treatment. Surfaces to which this agent had been applied have been shown to kill 3.3- to 4.3-log₁₀ *S aureus* and 2.2- to 4.8-log₁₀ *Pseudomonas aeruginosa* hours after application of Surfacine.³⁴ In addition, a greater than 3-log₁₀ kill of MRSA and VRE was also achieved. Residual activity of Surfacine against VRE has been shown for 13 days.³³ However, to date there are no published studies assessing the ability of this agent to reduce the microbial contamination on environmental surfaces in actual hospital rooms or to decrease the incidence of health care-associated infections. Silver is made by complexing alkaline earth metals with crystal aluminosilicate, which is partially replaced by silver ions using ion exchange method. The antibacterial efficacy of a silver/zinc zeolite ceramic coating on stainless steel has been demonstrated by challenge with *S aureus*, but to date there are no studies of actual hospital surfaces coated with a silver/zinc zeolite.³⁵ The effectiveness of silver nanoparticles when incorporated into environmental surfaces has not been assessed in the hospital environment.

Copper

Copper is an essential trace element in most living organisms, and more than 30 types of copper-containing proteins have been described.³⁶⁻⁴⁰ Copper has been used for centuries as a medicinal and to prevent growth of barnacles on the hulls of ships.^{37,38} However, copper ions at increased levels are toxic to most microorganisms because of their ability to generate reactive oxygen species and act as a strong soft metal (eg, leading to release of iron from Fe-S clusters).^{37,39} The copper generated radicals can damage lipids, nucleic acids, and proteins, leading to cell death. In health care, copper compounds (ie, copper-silver ionization) are used for control of *Legionella* species in water supplies⁴¹ and *Aspergillus* on building materials (ie, copper-8-quinolinolate).⁴² More recently, copper-coated or -impregnated surfaces have been evaluated in hospitals.^{37,39,40}

The contact killing of microbes by copper has been assessed in multiple in vitro studies.^{38,40} Most microbes were inactivated by copper within minutes to hours, but, because parameters such as inoculation technique, incubation temperature, and copper content of the alloy were not investigated in a systematic way, comparisons between studies are difficult.³⁸ According to Grass et al, a few general principles can be drawn from these in vitro studies: higher copper content of alloys, higher temperature, and higher relative humidity increased the efficacy of killing.³⁸ Treatments that

lowered corrosion rates (eg, application of corrosion inhibitors or a thick copper oxide layer) lowered the antimicrobial effectiveness of copper surfaces. Contact with copper has been demonstrated to kill a variety of health care-associated pathogens including *S aureus*, MRSA, *Enterococcus* species, *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *P aeruginosa*, and *Mycobacterium tuberculosis* in minutes to several hours.^{38,43}

Spore-forming bacteria such as *Bacillus* and *Clostridium* pose a substantial challenge to germicides that work by contact killing because spores are relatively resistant to heat, radiation, desiccation, and germicides. Copper has been shown to kill greater than 6-log₁₀ of vegetative *C difficile* cells within 30 minutes.⁴⁴ However, the same authors demonstrated no reduction in viability of dormant *C difficile* spores within 3 hours, although a greater than 99% reduction of germinating *C difficile* spores was noted at 3 hours. Greater than 3-log₁₀ of *C difficile* spores have been shown to be completely inactivated by copper surfaces in 24 to 48 hours.⁴⁵

As with silver, microorganisms have developed mechanisms to survive copper ion challenge including efflux pumps, permeability barriers, intra- and extracellular sequestration, enzymatic detoxification, and reduction in the sensitivity of cellular targets to copper ions.^{36,40} Some strains of bacteria isolated from copper coins have been demonstrated to survive for more than 48 hours on dry copper surfaces.⁴⁶ However, contact with copper alloys will kill most copper ion-resistant strains (eg, *Salmonella enterica* pv typhimurium, *E coli*, *P aeruginosa*) within 60 minutes although one strain of *Enterococcus faecium* survived for greater than 2 hours on a dry copper surface.³⁷

Multiple studies of copper containing surfaces or devices have been conducted in the health care setting comparing the level and frequency of surface contamination to control surfaces.⁴⁷⁻⁵¹ Studies have either used concurrent non-copper-containing control surfaces⁴⁷⁻⁵⁰ or a crossover design.⁵¹ Casey et al demonstrated that a copper toilet seat would result in a 94% to 98% reduction in total aerobic colony-forming units (cfu).⁴⁷ In a similar study, it was demonstrated that copper-coated desks, trolleys, and surfaces (top of cupboard and windowsill) resulted in a 1- to 2-log₁₀ decrease in mean cfu.⁴⁸ Rai et al have demonstrated that copper coating of the arms of phlebotomy chair and tray over the chair reduced median total aerobic cfu by 88% and 90%, respectively.⁵⁰ Mikolay et al demonstrated a 37% reduction of total aerobic cfu on door knobs, push plates, and light switches.⁴⁹ Finally, Karpanen et al have described the surface contamination levels on 14 types of frequently touched items made of copper alloys that were installed in various locations on an acute medical ward.⁵¹ Items included door handles, toilet seats, grab rails, light switches, over-bed tables, commodes, and others. The copper items were switched to similar non-copper items halfway through the 24-week study period. Eight of the 14 copper item types had significantly lower microbial counts on their surfaces compared with those made of standard materials. MRSA, VRE, coliforms, and *C difficile* were found to contaminate 0.4% to 8.1% of surfaces; contamination by VRE and coliforms was statistically reduced on the copper items, and no significant reduction was noted for MRSA and *C difficile*. Repeated cleaning/disinfection of a copper surface over 5 days with either 1% sodium hypochlorite or 70% industrial methylated spirit were shown to lead to "surface conditioning," which resulted in decreased killing of *S aureus*.⁵² In interpreting the results of some of the above studies, it is important to note that neither the study by Rai et al⁵⁰ nor that of Karpanen et al⁵¹ assessed the thoroughness of cleaning of surfaces, thus the finding may have been due to improved cleaning rather than the effect of copper on decreasing bioburden. Copper-containing paints,⁵³ fabrics,⁴⁰ hand rubs,⁴⁰ microfiber cleaning cloths,⁵⁴ pens,⁵⁵ and fins within air-conditioning units⁵⁶ have also been evaluated for use in health care.

SURFACES IMPREGNATED OR COATED WITH A GERMICIDE

Surfaces and devices impregnated or coated with a germicide are widely available. Concern has been raised that the use of such surfaces and devices might lead to bacteria developing resistance to the germicide with possible cross-resistance to clinically useful antibiotics.^{57,58}

Triclosan

Triclosan (2,4,4'-trichloro-2'-hydroxy-diphenyl ether) is a non-ionic, colorless substance that has antimicrobial activity at concentrations of 0.2% to 2%.⁵⁹ Triclosan has a broad range of antimicrobial activity, but it is often bacteriostatic.⁵⁹ Its activity against gram-positive organisms is greater than its activity against gram-negative bacilli. Triclosan has been incorporated into a wide range of home and personal care objects, including soaps, underarm deodorants, toothpaste, and cutting boards.^{58,60} Triclosan-impregnated cutting boards have been shown to lead to decreases in bacteria applied to the boards, including reductions of 0.5- to 1.0-log₁₀ for *S aureus* and *Serratia* species and 1.5- to 1.7-log₁₀ for *E coli* and *Salmonella* species.⁶¹ *P aeruginosa* is intrinsically resistant to triclosan.⁶² When *P aeruginosa* was grown as biofilm on discs of polyethylene, Teflon, and stainless steel, 1% triclosan was only effective in achieving a reduction in organisms of less than 1-log₁₀.⁶³ In the laboratory, bacteria with reduced susceptibility to triclosan can be produced fairly readily by serial passage in increasing triclosan concentration.⁶² However, the minimum inhibitory concentration of such strains generally are substantially below the concentration of triclosan contained in antimicrobial products. We were unable to find any studies evaluating the use of triclosan-impregnated hospital environmental surfaces or devices.

Quaternary ammonium compounds

Recently, an antimicrobial surfactant whose core product is a quaternary ammonium salt, Goldshield, has been evaluated.⁶⁴ Using a carrier test, the agent was demonstrated to kill 0.5- to 2.4-log₁₀ MRSA and 0.6- to 0.9-log₁₀ *P aeruginosa* and *E coli* within 30 minutes on formica and stainless steel.⁶⁴ Rechallenge after 4 days generally did not demonstrate microbial inactivation, although a statistical reduction was noted for MRSA on formica (but not stainless steel) carriers. No published studies are available on using this agent on environmental surfaces in hospital rooms. Data demonstrate that quaternary ammonium disinfectants continue to have persistent antimicrobial activity that extends beyond their wet time on the surface; activity may extend beyond 24 hours provided the disinfectant is left on the surface undisturbed.⁶⁵

MISCELLANEOUS METHODS TO ACHIEVE SELF-DISINFECTING SURFACES

Several promising new technologies are under examination to develop self-disinfecting surfaces including altered surface typography and light-activated germicides bound to surfaces.

Altered topography

A novel approach to the development of self-disinfecting surfaces is the use of an engineered microtopography to inhibit bacterial biofilm formation. One such design is Sharklet AF (Sharklet Technologies, Alachua, FL), which seeks to use topography similar to shark skin to inhibit biofilms. Reduced biofilm formation and growth of *S aureus* has been described on molds employing Sharklet AF.⁶⁶ Urogenic *E coli* were inhibited on silicone elastomer

Table 2
Advantages and disadvantages of currently proposed self-disinfecting surfaces in hospital rooms

Advantages
<ul style="list-style-type: none"> • Provides continuous disinfection of environmental surfaces • Does not depend on adequacy of cleaning/disinfection by environmental service workers • Broad-spectrum antimicrobial activity • Very low or no toxicity to humans
Current limitations
<ul style="list-style-type: none"> • Impossible to impregnate or coat all possible room surfaces and medical devices used in a hospital room • Efficacy of self-disinfecting surfaces to decrease health care-associated infections has not been demonstrated in a clinical trial • Cost of purchasing and installing self-disinfecting surfaces has not been published • Possible development of resistance by microbes to the self-disinfecting method • In general, modest reductions in surface contamination (ie, 1- to 2-log₁₀) demonstrated • Durability with repeated cycles of cleaning and disinfection not yet evaluated

coupons, suggesting that this method could be used to develop Foley catheters, which would inhibit microbial growth.⁶⁷ We are unaware of any published studies assessing this new technology to inhibit microbial growth on actual indwelling medical devices or hospital environmental surfaces.

Light-activated antimicrobial coatings

Light-activated antimicrobial coatings are currently being studied for the continuous disinfection of surfaces. Irradiation of certain compounds (photosensitizers) with visible light results in the production of cytotoxic species such as singlet oxygen and free radicals. Wilson studied a cellulose acetate layer containing the photosensitizer toluidine blue O and demonstrated kills of 94% for *S aureus* and 99.9% for *P aeruginosa* when in contact with impregnated acetate layer following exposure to light (400–700 nm wavelength) for 24 hours.⁶⁸ More recently, a cellulose acetate coating containing toluidine blue O and rose Bengal has been studied.^{69–71} Illumination of 6 hours resulted in a 2- to 3-log₁₀ reduction in *S. aureus*, but, if the organism was suspended in saliva or horse serum, reductions of <1-log₁₀ were noted.⁶⁹ Exposures of ≥6 hours have been demonstrated to inactivate >6-log₁₀ of *S aureus*, MRSA, *E coli*, and *C difficile* (mainly vegetative cells) under experimental conditions.⁷⁰ In a clinical environment, a 63.8% reduction in aerobes and 81.8% reduction in anaerobes have been reported.⁷¹ Silicone polymers containing the light-activated antimicrobial agent methylene blue were more effective in reducing the microbial load on surfaces in a clinical environment when combined with gold nanoparticles.⁷²

CONCLUSION

The novel technologies, especially those employing nanotechnology, has dramatically improved the likelihood of developing a self-disinfecting surface. The potential development of such surfaces has tremendous possibilities. Most importantly, the use of such surfaces could minimize the impact of poor cleaning and disinfecting practices during both routine and terminal room cleaning and disinfection. It is important to note that the currently available “no-touch” technologies such as UV-C light irradiation and vaporized/aerosolized hydrogen peroxide can only be used for terminal room disinfection at the present time because they are hazardous to patients and staff. However, novel “no touch” methods such as using continuous low-dose (ie, 0.2 ppm) hydrogen peroxide vapor or high-intensity, narrow-spectrum (ie, 405 nm)

visible light are being evaluated.^{73,74} The potential advantages and current limitations of self-disinfecting technologies are summarized in Table 2. Of the different technologies available (Table 1), copper-impregnated or -coated surfaces have been the most extensively evaluated.⁴⁰

However, a few cautions regarding self-disinfecting surfaces should be noted. First, many of these surfaces have demonstrated only modest killing (<2-log₁₀ pathogens). Second, the ability of these new surfaces to kill intrinsically more resistant pathogens such as *C difficile* spores and norovirus has often not been fully evaluated. Third, the cost of installing and maintaining such surfaces has not been described. Fourth, only incomplete information is available on the durability of such surfaces and whether their antimicrobial activity is affected by temperature, humidity, frequency of cleaning, and presence of organic load. Fifth, the relative benefits and limitations of different self-disinfecting technologies have not been studied in comparative trials. Finally, no studies have been published that demonstrate that installing such surfaces reduces health care-associated infections. In addition, it is important to note that the level of microbial contamination of hospital room surfaces does not correlate with the frequency with which they are touched by HCP, suggesting that, for self-disinfecting surfaces to reduce health care-associated infections, multiple self-disinfecting surfaces and devices would need to be installed.⁷⁵ Despite the current unknowns with regard to the utility of self-disinfecting surfaces, continued research and evaluation of clinical value in this area are clearly warranted as means of reducing the impact of environmental contamination in the transmission of health care-associated pathogens.

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