Abstract Despite considerable efforts, healthcare-associated infections (HAIs) continue to be globally responsible for serious morbidity, increased costs and prolonged length of stay. Among potentially preventable sources of microbial pathogens causing HAIs, patient care items and environmental surfaces frequently touched play an important role in the chain of transmission. Microorganisms contaminating such high-touch surfaces include Gram-positive and Gram-negative bacteria, viruses, yeasts and parasites, with improved cleaning and disinfection effectively decreasing the rate of HAIs. Manual and automated surface cleaning strategies used in the control of infectious outbreaks are discussed and current trends concerning the prevention of contamination by the use of antimicrobial surfaces are taken into consideration in this manuscript.

Introduction

In spite of the growing global commitment towards an effective reduction of healthcare-associated infections (HAIs), it is unfortunately certain that such infections will continue to be responsible for very high morbidity, increased costs and length of stay (LOS) for the coming decades [1, 2].

Among potential sources of pathogens causing HAIs, the most frequent are the patient’s microbiota and the hands of healthcare personnel [3]. Additionally, evidence that high-touch surfaces (HTS) will work as an extra source of microbial pathogens accumulated over the years, e.g., several microorganisms can survive on medical equipment for hours to months, improved cleaning and disinfection of surfaces decrease the rate of HAI, and hospital environmental screening results and the study of clonal outbreaks, all have given support to the role of contaminated HTS in the transmission of pathogens between patients and healthcare personnel [4]. From surfaces, microbial transmission may occur either through direct patient contact or, indirectly, through healthcare personnel hands or gloves [5]. Therefore, upon potentially preventable sources of microorganisms, contaminated HTS deserve strong consideration.

Microbial pathogens most frequently involved in the contamination of hospital environmental surfaces are (methillin-resistant) *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *Clostridium difficile*, multidrug resistant Gramme-negative bacilli (such as *Pseudomonas, Acinetobacter* and *Enterobacteriaceae*), Norovirus, Coronavirus and *Candida* species [6–10].

Strategies for cleaning contaminated HTS may include manual and automated techniques. Wipes and cloths with application of detergents or disinfectants are examples of manual techniques, while automated methods may involve UV light, hydrogen peroxide, steam vapour, ozone and HINS (high-intensity narrow-spectrum light). On the other side, in order to prevent contamination of HTS, antimicrobial surfaces are being developed. The inhibition of microbial adhesion with repellent films is a possible strategy, as it is the surface treatment with antimicrobial
coatings of silver, copper, polycations, triclosan, bacteriophages or, even, light-activated biotoxic radicals.

The aim of this manuscript is to review the role of high-touch surfaces in healthcare-associated infections, from the aetiology to strategies for surface cleaning and addressing preventive trends.

**Types of surfaces**

As early as 1972, Spaulding proposed a classification of inanimate surfaces into three general categories based on the risk of infection if the surfaces were contaminated at the time of use [11]. These categories can be applied to devices or instruments as follows: critical (exposed to normally sterile areas of the body; require sterilization), semi-critical (touch mucous membranes; may be sterilized or disinfected), and non-critical (touch skin or come into contact with people only indirectly; can be either cleaned and then disinfected with an intermediate-level disinfectant, sanitized with a low-level disinfectant or, simply, cleaned with water and soap). In 1991, the CDC proposed environmental surfaces (floors, walls and other “housekeeping surfaces” that do not make direct contact with a person’s skin) as an additional category [12]. More recently, the CDC’s and Healthcare Infection Control Practices Advisory Committee’s Guidelines for Environmental Infection Control in Healthcare Facilities [13] divided surfaces into patient care items and environmental surfaces. Environmental surfaces were further divided into medical equipment and patient room surfaces (Table 1).

Over the years, research has been done in order to better target room disinfection practices. Following recommendations made by the CDC to clean and disinfect HTS more frequently than minimal-touch surfaces, data published in 2010 by Huslage et al., based on the real frequency of contact, defined the top five most touched surfaces in hospitals: bed rails, bed surface, supply cart, over-bed table and intravenous pump [14]. HTS may be classified as non-critical items (the contact occurs with intact skin that effectively acts as a barrier to most pathogens, but not with mucous membranes) and must be subject to cleaning and disinfection procedures as recommended, but with no absolute need for sterilization [15].

**Microbial pathogens**

Many pathogens may thrive on healthcare-associated equipment and environmental surfaces. Among such organisms, MRSA, VRE, *C. difficile*, *P. aeruginosa*, *A. baumannii*, *Enterobacteriaceae*, *Stenotrophomonas maltophilia*, *Burkholderia cepacia*, Norovirus, Coronavirus and *Candida* spp. may persist and contribute to the infection risk to which patients are systematically exposed.

**Methicillin-resistant *Staphylococcus aureus***

Several studies have demonstrated that basic cleaning leads to MRSA elimination from environmental surfaces and enhanced cleaning may terminate outbreaks in intensive care units, with cost savings of $45,000 up to $51,000 per year [16–19]. Recently, two studies reported positively about pulsed xenon UV and hydrogen peroxide methods to boost the decontamination of patient rooms, contributing towards a reduction of MRSA bioburden [20, 21].

**Vancomycin-resistant enterococci**

Its inherent ability to resist certain antimicrobial agents (such as cephalosporins and aminoglycosides) allied to a great capacity to acquire determinants of antibiotic resistance (like gene clusters of vancomycin resistance) turn enterococci into a versatile nosocomial multidrug-resistant pathogen. The number of VRE infections has been increasing worldwide, most frequently afflicting patients with serious comorbidities or undergoing prolonged hospitalization [22].

VRE are known to survive for a long time in the hospital environment. Viability on surfaces may range from 5 days to 4 months [23]. Moreover, enterococci are tolerant to heat, chlorine and some alcohol preparations, making them very resilient to conventional cleaning practices, thus becoming easily disseminated among healthcare facilities [24]. Therefore, besides thorough environmental cleaning several times a day with disinfectants, VRE management protocols should include strict adoption of contact precautions and implementation of comprehensive educational programs for staff [25, 26].

**Clostridium difficile**

Spores of *C. difficile* can hold on to a healthcare environment for more than 5 months [23, 27]. Fortunately, the use of chlorine-releasing disinfectants reduces the amount of spores in the environment, with some evidence suggesting that it may reduce the risk of recurrence and transmission of *C. difficile*-associated infections [28].

**Pseudomonas aeruginosa**

Transmission of *P. aeruginosa* may easily occur from contaminated sinks to hands of healthcare personnel during washing, since this organism may thrive in biofilms that are adherent to sink traps, pipes, water lines and hospital drains [29], turning these fashion-organized bacteria more prone to resist to disinfectants [30]. Additionally, *P. aeruginosa* can resist 6 hours to 16 months on dry inanimate surfaces [23]. Programs to control transmission should include, therefore, repeated cleaning with chlorine-based disinfectants, physical removal of persistent...
biofilm, replacement of components whenever feasible and regular inspection [31, 32].

Acinetobacter baumannii

The increase in the number of HAIs caused by A. baumannii might be explained not only by its ability to persist from 5 days to more than 5 months in undisturbed surfaces of healthcare equipment [23], but also by its high resilience to cleaning with conventional detergent and alcohol disinfectants [33]. Hence, outbreaks in hospital or other healthcare settings are difficult to contain because of the easy environmental contamination by this pathogen [34–36]. Targeted infection control measures may be needed, including intensive cleaning with sodium hypochlorite and subsequent measurement of cleanliness, hand hygiene training, adoption of barrier precautions and contact isolation, as well as patient surveillance [37, 38].

Enterobacteriaceae

There has been a growing concern about Klebsiella pneumoniae infections, mainly because of its extensive \(\beta\)-lactamase resistance. K. pneumoniae are usual colonizers of the human gastrointestinal tract, pharynx and skin that may cause wound infections, pneumonia and sepsis, particularly in immunocompromised patients [39]. More recently, given its wide dissemination and selective advantage to resist to carbapenem antibiotics, K. pneumoniae have been showing a propensity to cause outbreaks in healthcare institutions [40]. It is known that K. pneumoniae may survive for more than 30 months in the healthcare environment [23] and that the origin of some outbreaks has been related to sinks and related pipes [41, 42].

Another member of the Enterobacteriaceae family, Serratia marcescens, are known to cause pneumonia, meningitis, urinary tract and bloodstream infections. MDR isolates, including colistin resistant [43], have been responsible for serious outbreaks among intensive care units and critically ill neonates [44–46]. S. marcescens are known to survive up to 2 months on dry inanimate surfaces [23] and have frequently been recovered from water pipes and hospital disinfectants [47].

Because of the easy transmission and environmental persistence of Enterobacteriaceae in healthcare facilities, adequate solutions aiming its eradication should ensure comprehensive educational interventions, hand hygiene training, chlorine-based cleaning and even the replacement of sinks and pipes [42, 48, 49].

## Table 1: Types of healthcare-associated surfaces

| Patient care items              | Blood pressure cuff            |
|--------------------------------|--------------------------------|
|                                | Pulse oximeter                 |
|                                | Thermometer                    |
|                                | Glucometer                     |
|                                | Stethoscope                    |
|                                | Venipuncture tourniquets       |
| Environmental surfaces         | Medical equipment              |
|                                | Monitor touch screen, controls and cables |
|                                | Ventilator control panel       |
|                                | Oxygen flow meter and suction regulator |
|                                | Intravenous pump control and pole |
|                                | Supply cart                    |
| Patient room                   | Bed rails/controls             |
|                                | Bedside table/controls         |
|                                | Over-bed table                 |
|                                | Chair                          |
|                                | Call box/button                |
|                                | Telephone and TV remote        |
|                                | Privacy curtain                |
|                                | Window blinds and control      |
|                                | Light switches                 |
|                                | Door and closet knobs/plates   |
|                                | Toilet seat, flush handle and bedpan cleaner |
|                                | Sinks and soap dispensers      |
|                                | Handrails                      |
|                                | Trash can                      |

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Stenotrophomonas maltophilia

Similarly to other bacteria, it can persist in biofilms that may turn cleaning products and disinfectants more ineffective [30]. Long-term control of *S. maltophilia* will be dependent upon the integration of an efficient cleaning strategy into a targeted healthcare facilities maintenance program [50].

Burkholderia cepacia

It is widely distributed in soil and water habitats and recent healthcare-associated outbreaks have been linked to *B. cepacia* persistence in disinfectants, drugs, medical devices (e.g., respiratory nebulizers), sinks and contiguous aerator filters [51–53]. Strict and repeated cleaning and replacement of aerators with flow straighteners may be required to stop outbreaks [51, 54].

Norovirus

The origin of Norovirus outbreaks in healthcare facilities has been traced not only to sites near bathroom showers and toilets but also to sites near patients, including clinical equipment (e.g., blood pressure and pulse oximeter monitors), thermometers, trolleys and soap and alcohol gel containers [55]. After suspected or confirmed case contact, use of soap and running water is recommended [56], probably with a superior efficacy than ethanol-based sanitizers [57]. However, detergent-based cleaning may be insufficient to eliminate Norovirus from the environment and, therefore, hypochlorite solutions of at least 1000 ppm for an appropriate contact time represent a better strategy for cleaning [56, 58].

Coronavirus

Human Coronavirus, usually responsible for acute respiratory syndromes, have been causing increased concern due to contact transmission during healthcare-associated outbreaks. Viral persistence on doorknobs and surgical boom shelves has already been identified, with a presumed viability of 48 h; scrupulous environmental cleaning is certainly highly advisable in reducing the spread [59, 60]. Moreover, biocidal surfaces based on copper alloys are very effective in inactivating Coronavirus and could be employed in high touch surfaces in order to prevent the transmission of this respiratory virus [61].

Candida

Although *Candida* spp. are more resistant to germicidal chemicals than most vegetative bacteria, there are no specific recommendations other than general healthcare surface decontamination with disinfectants. Nevertheless, in order to control a recent outbreak by a MDR *C. auris*, measures implemented included isolation of cases and contacts, protective clothing, screening of all other ward patients, skin decontamination with chlorhexidine, environmental cleaning with chlorine-based disinfectants and hydrogen peroxide vapour [62]. A clinical alert issued in June 2016 by the CDC on the global emergence of invasive infections caused by the MDR *C. auris* recommended thorough daily and terminal cleaning and disinfection of patient rooms using an EPA-registered hospital grade disinfectant with a fungal claim.

Preventing the environmental surface transmission of healthcare-associated pathogens

General strategies

Based on patterns of microbial resistance to physical and chemical germicidal agents and on the instrument/surface classification, Spaulding has proposed three levels of disinfection [11]: high-level disinfection, that inactivates all vegetative bacteria, mycobacteria, viruses, fungi and some bacterial spores by the action of chemicals such as glutaraldehyde, peracetic acid and hydrogen peroxide; intermediate-level disinfection, which is effective against vegetative bacteria, some spores, mycobacteria, fungi, lipid and medium size viruses, but not against all nonlipid and small size viruses (e.g., sodium hypochlorite, alcohols, some phenolics and some iodophors); and low-level disinfection, that inactivates vegetative bacteria, fungi, enveloped viruses and some non-enveloped viruses (e.g., adenoviruses) by the action of quaternary ammonium compounds, some phenolics and some iodophors [12].

In order to prevent the persistence of microbial pathogens on medical equipment and environmental surfaces, education of healthcare staff, checklists and assessment of the adequacy of cleaning (by direct observation, use of fluorescent markers, of ATP bioluminescence systems, swab cultures or agar slide cultures) with feedback to the staff are general interventions that need to be implemented to improve the frequency of adequate cleaning [63–65].

Strategies for high-touch surfaces

Patient care items

As general principles, all patient care items should be cleaned and/or decontaminated before and after use, for all patients [66, 67]; whenever these items come into contact with blood or other body fluids, stringent cleaning and disinfection is warranted before and after use [68].

Manufacturers of medical equipment usually provide care and maintenance instructions regarding servicing decontamination, compatibility with germicidal agents and water-resistance. In the absence of such instructions, the CDC and the
Healthcare Infection Control Practices Advisory Committee (HICPAC) recommend non-critical medical equipment (e.g., stethoscopes, blood pressure cuffs, equipment knobs and controls) to be subject to low or intermediate-level disinfection after cleansing, depending on the nature and degree of contamination. For instance, ethyl or isopropyl alcohol (60–90% v/v) may be used to disinfect small surfaces (e.g., rubber stoppers of multiple-dose medication vials and thermometers) and surfaces of healthcare equipment (e.g., stethoscopes and ventilators) [69], while for large surfaces it may be impractical due to the rapid evaporation of alcohol and absence of the adequate contact time [12].

Environmental surfaces

As a whole, frequently touched environmental surfaces benefit from enhanced cleaning. Routine decontamination and disinfection are practices normally included within institutional cleaning policies. Nevertheless, evidence has been built in order to favour the use of less toxic detergents over disinfectants in non-outbreak situations, without losing cleaning efficacy or adding costs [70]. Detergents are less likely to contribute to the accumulation or dispersal of tolerance or resistance genes among healthcare-associated microbial isolates [71, 72].

According to the CDC, for medical equipment (particularly in the case of monitor touch screens, controls and cables), a disposable plastic barrier protection can be useful whenever these surfaces, touched frequently by gloved hands, may become contaminated with body fluids or present difficulties to cleaning.

Manual cleaning

The physical removal of soil is a very important step in the cleaning process since its presence will impede the microbicidal activity of disinfectants, if needed. In order to control the bioburden on regular wards, daily cleaning with neutral detergent wipes is usually sufficient. However, more attention is essential on high-risk intensive care units because of the easiness of microbial recontamination [73]. Moreover, patients colonized or infected with specific pathogens may demand cleaning regimens with disinfectants with registered label claims [68].

After patient discharge, terminal or deep cleaning is usually performed by removal of all detachable objects from the room and systematically wiping all surfaces downward to the floor level, with detergent cloths or disinfectant wipes.

New liquid disinfectants are under development and include: improved hydrogen peroxide disinfectants, effective in reducing bacterial levels on surfaces [74, 75], related to fewer HAIs [76] and able to reduce contamination by MDR pathogens on soft surfaces such as bedside curtains [77]; peracetic acid and hydrogen peroxide disinfectants, a sporicidal combination that was shown to lower bacterial levels on surfaces and to reduce the contamination by MRSA, VRE and C. difficile as effectively as sodium hypochlorite [78]; electrolyzed water (hypochlorous acid) disinfectant, which may reduce bacterial levels on surfaces near patients in a higher degree than quaternary ammonium disinfectants [79]; further promising, electrolyzed water has been sprayed onto medical equipment (with a short contact time and without the need for wiping because no toxic residue remains on surfaces) with a reduction of aerobic bacteria and C. difficile spores [80]; cold-air atmospheric pressure plasma systems, which generate reactive oxygen species (ROS) with bactericidal activity and have potential use as surface disinfectants [81, 82]; nebulized polymeric guanidine, under investigation for its antimicrobial activity against several healthcare-associated pathogens [83].

Together with disinfectants, novel materials for liquid application such as microfiber cloths or mops and ultramicrowave cloths are under development. When used according to manufacturers’ instructions, an increased cleaning efficacy is to be expected as compared to standard cotton cloths or mops [84].

Automated cleaning

On the pathway to improve quality and ease of cleaning environmental surfaces, considerable efforts have been dedicated towards the development of automated devices. However, because of yet unsolved safety risks, mainly for patients, automated solutions are invariably targeting terminal cleaning. In most instances, these solutions do not preclude preliminary manual cleaning of surfaces to remove residual debris and reduce the bioburden.

The microbicidal effect of UV light has been in use for disinfection of environmental surfaces, instruments and air. By damaging the molecular bonds in DNA, a reduction in contamination by MRSA, VRE and C. difficile on high-touch surfaces has been achieved [85]. Automated mobile UV light devices are easy to use, with minimal need for special staff training. Nonetheless, several issues have been raised that may hinder its efficacy, namely, the time and intensity of light exposure and potential barriers that may exist between the lamp and its target surface. As such, UV light is regarded as an effective adjunct, but not a stand-alone strategy for disinfection [86].

By producing free radicals that lead to oxidation of DNA, proteins and membrane lipids [87], vapour and aerosol hydrogen peroxide systems have already been shown to be effective against MRSA, VRE, MDR Gramme-negative bacilli, C. difficile, viruses and fungi [88–93]. This excellent wide spectrum antimicrobial activity is not without drawbacks, such as toxicity after accidental exposure, minor erosion of environmental polymers and damage of electronic equipment. In addition, there is the need for trained operators, long cycle times for disinfection and the cost is high [94]. Experiments suggest that vapour-phase hydrogen peroxide is a more potent oxidizer of protein than liquid-phase hydrogen peroxide [87] and, when supplementing other strategies, microcondensation hydrogen peroxide vapour systems may have
contributed to control outbreaks by MRSA, MDR Gramme-negative bacteria and *C. difficile* in intensive care units, surgical wards and long-term care facilities [89, 95–99]. A novel silver-stabilized hydrogen peroxide is under investigation for its enhanced biocidal activity towards Gramme positive and negative bacteria capable of producing catalase, both in planktonic and biofilm cultures. Silver probably helps to stabilize and target hydrogen peroxide to the bacterial cell surface acting, therefore, synergistically [100]. In fact, a previous report on the effect of a dry-mist system using a mixture of hydrogen peroxide (5%) and silver cations (<50 ppm) was effective in decontaminating burn patient rooms, as well as a fungal research laboratory: a reduction in growth of at least two log was observed for tested bacteria, mycobacteria and fungi [101].

Steam cleaning is a non-toxic and rapid method that may reduce the total bioburden from environmental surfaces by more than 90% [102], with effectiveness against MRSA, VRE and Gramme-negative bacilli [103]. Concerns about security when steam is applied to electrical items such as switches and buttons and risk of burns and scalds when cleaning a crowded ward are the reasons precluding its widespread use in healthcare facilities [104].

The oxidizing capacity of ozone justifies its previous evaluation as a gaseous decontaminant for controlling *C. difficile* on environmental surfaces and *E. coli* in hospital laundries [105, 106]. While it seems highly effective against vegetative bacterial cells, a smaller impact has been found in case of bacterial spores and fungi [107]. Moreover, corrosiveness and toxicity issues may restrain further the use of ozone in healthcare settings [108].

By targeting intracellular porphyrins that absorb the light and produce ROS with bactericidal activity [109], high-intensity narrow-spectrum (HINS) light stands as another light-based method with possible application for decontamination of high-touch surfaces, although its efficacy is lower than UV light. As clear advantages, HINS light is safe for patients, allowing continuous decontamination of the clinical environment [110] and it exhibits a wide-range microbicidal activity that includes MRSA, *P. aeruginosa* and *A. baumannii* [111, 112]. However, HINS light has yet to prove its effectiveness in clinical settings and benefits upon HAI rates, given the small range of published studies [110, 112, 113].

**Antimicrobial surfaces** Instead of focusing on the reduction of the bioburden on surfaces solely by cleaning, there are solutions designed to prevent surfaces from working as a microbial reservoir and that may be used as an adjunct to other strategies in reducing HAIs.

Antiadhesive surfaces target microbial adhesion usually by the interaction of antagonist physicochemical properties. Easy-clean surfaces that are hydrophobic repel bacteria better than glass-coated controls [114], while hydrophilic surfaces favour water sheeting and subsequent cleaning. Similarly, polyethylene glycol coated surfaces promote a hydrophilic interaction against bacteria, preventing attachment [115]. The use of diamond-like carbon films has already been tried for medical implanted devices such as joint prostheses and stents in order to repel microbial adhesion [116]. Despite being non-toxic and appealing, the lack of biocidal properties may turn discouraging a more generalized implementation of such easy-clean technologies.

Currently, there are available antimicrobial coatings that can produce a microbicidal effect and could lead to an effective reduction of high-touch surface bioburden. For instance, inorganic metals have been investigated for a long time and it is known that silver binds with disulphide and sulphydryl groups present in proteins of microbial cell wall leading to death [117], inhibiting not only environmental contamination but also colonization of medical implanted devices [118, 119]; copper and copper alloys may form reactive oxygen radicals that damage nucleic acid and proteins [117] and have already demonstrated a potent antimicrobial effect when applied to surfaces, reducing the rate of healthcare-associated infections [120, 121]. Polycationic surfaces, such as those coated with polyethyleneimines, hydrophobically attract and kill bacteria by physically damaging the cell wall [122]. Triclosan has been in use for more than 30 years in detergents, soaps and cosmetics. At lower concentrations, it is bacteriostatic by inhibiting an enzyme involved in fatty acid synthesis and, at higher concentrations, it is bactericidal by destabilizing microbial membranes. Compatibilization of triclosan with polymers may extend the duration of its wide-spectrum antimicrobial activity [123] and could prove effective in reducing environmental surface load of pathogens. Bacteriophages applied to surfaces and targeting specific microorganisms have been attempted and mixtures of phages have been further suggested in order to effectively reduce the environmental bioburden. Particularly interesting in healthcare settings is the fact that MDR pathogens keep vulnerable to the lytic action of phages [124, 125]. Light-activated antimicrobial surfaces, such as those coated with titanium dioxide and activated by UV light [126], generate reactive oxygen radicals with nonselective toxicity towards both bacteria and yeasts [127]. Similarly, photosensitized surfaces could reduce the healthcare bioburden without promoting microbial drug resistance mechanisms. Although antimicrobial coatings may seem very promising, especially as an adjunct measure to more traditional and proven cleaning strategies, some concerns keep hindering its wider use in healthcare settings. Robust cost-effectiveness studies are still lacking since reliable information about antimicrobial coatings durability, resistance and possible toxicity is yet somewhat insufficient [50, 68].
Conclusion

Given the high morbidity and costs associated with HAIs, improved strategies are urgently needed to reduce effectively the rate of infection. Certainly, one good step forward would be the blockade of transmission from environmental high-touch surfaces. At the moment, manual and automated techniques for cleaning surfaces exhibit variable success. Concerns over durability, resistance and toxicity may be precluding a much wider application of the novel antimicrobial coatings. Admitting an albeit limited performance of the traditional cleaning methods, the supplementation with newer technology should be indicated. Hence, more randomized controlled trials and cost-effectiveness studies are needed and further investigation on antimicrobial surfaces is welcomed in order to face the challenge imposed by the global advance of antimicrobial drug resistance and the pressure to reduce bed turnover times with shortages in nursing personnel, housekeeping staff and budgets.

Compliance with ethical standards

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