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The role of the hospital environment in the healthcare-associated infections: a general review of the literature

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Abstract. – Healthcare-associated infections (HAIs) are one of the most relevant public health problems worldwide. The role of the hospital environment as a reservoir of pathogens causing HAIs is still debated. These pathogens are common in several hospital environments, where they are able to persist from hours to months and their circulation is favored by healthcare workers (HCWs). Hospital surfaces at close contact with patients such as bed bars and header, bedside table, taps, and handles in wards ("high-touched sur-faces"), are considered easily contaminable and at risk to transfer pathogens to patients. However, some studies showed the possible role played by "non-classical" surfaces such as healthcare workers' (HCWs) mobile phones and personal computers as well as oxygen humidifiers and protective lead garments used in operating rooms. HCWs' hands play a fundamental role in patient-to-patient transmission by touching contaminated surfaces or patients during care activities. The aim of this review is to evaluate the role of the hospital environment in the transmission of nosocomial pathogens, focusing on single pathogens caus-ing HAIs and the importance of hospital surfaces as reservoirs.

Key Words:
HAIs, Hospital environment, Gram-negative bacteria, Gram-positive bacteria.

Introduction

Nowadays, healthcare-associated infections (HAIs) represent one of the most relevant public health problems both in high-income and developing countries[1]. HAIs heavily influence many aspects of health care, such as patients' safety and economic burden[2-5]. In Italy, according to the National Health Institute, there are 450,000-700,000 HAIs per year, 30% of which could be prevented[6]. In recent years, there has been an increasing interest in the role played by contaminated hospital environment[7]. Many studies showed that the hospital environment could be accounted for the transmission of important nosocomial pathogens to patients. Among these nosocomial pathogens, there are methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *Clostridium difficile*, *Acinetobacter* spp. and *Norovirus*[8-24] which can be easily isolated within the hospital environment, especially nearby colonized or infected patients. These micro-organisms can persist in the environment for hours to days (and in some cases for months), and their circulation is facilitated by healthcare workers. Table I shows the survival in the hospital environment of principal pathogens causing HAIs.

A preventable risk factor for infection with MRSA, VRE, *C. difficile* or *Acinetobacter* spp is represented by the hospitalization in a room previously occupied by infected patients[13,14,25,26]. Easily infected surfaces are those closer to the patient, such as bed bars and header, bedside table, taps and handles in wards ("high-touched surfaces"). Moreover, some studies[27-34] demonstrated the role played in this transmission by "non-classical" surfaces, such as healthcare

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Table I. Environmental survival time of principal pathogens causing HAIs (modified by Kramer et al[21]).

Microorganisms	Environmental survival time
Gram-negative bacteria	
Escherichia coli	From 1.5 hours to 16 months
Pseudomonas aeruginosa	From 6 hours to 16 months
Klebsiella spp.	From 2 hours to 30 months
Acinetobacter spp.	From 3 days to 5 months
Gram-positive bacteria	
MRSA	From 7 days to 7 months
VRE	From 5 days to 4 months
Clostridium difficile	> 5 months
Fungi	
Candida albicans	From 1 to 120 days
Viruses	
Norovirus	From 8 hours to 7 days

workers' (HCWs) mobile phones and personal computers as well as oxygen humidifiers and protective lead garments used in operating rooms. Furthermore, several studies focused on the important role played by HCWs' hands in the pathogens transmission to patients. Especially, pathogens can colonize HCWs' hands by touching contaminated surfaces or contaminated/infected patients during care activities and, consequently, can easily transfer the microorganisms to other patients[35-37]. As a matter of fact, HCWs have frequent contacts with the environmental surfaces in patients' rooms and they can easily contaminate their hands and/or gloves in this way. It has been demonstrated that MRSA can contaminate with an equal frequency the HCWs' hands following the contact with either colonized/infected patients or only with contaminated surfaces[38]. Despite the high scientific evidence, the importance of contaminated hospital environment and its sanitation are still object of debate across the world[39]. A number of studies highlighted the importance of hospital cleaning in the reduction of HAIs[40]. However, while much of the evidence for cleaning is linked to outbreaks, a few studies focus on the impact of enhanced cleaning practices on the hospital environment in the routine situation[41]. This review aims to highlight the possible role of contaminated hospital environment in the transmission of HAIs and it focuses the attention on its role as reservoir and transmission of those pathogens widely considered the principal cause of HAIs.

The Role of the Hospital Environment Contamination in the Transmission of Different Nosocomial Pathogens

Gram-Negative Bacteria

Acinetobacter Baumannii

Over the last years, *Acinetobacter baumannii* has become one of the most important healthcare-associated pathogens. Many studies[42] reported that it is the cause of outbreaks of nosocomial infections including septicemia, bacteremia, ventilator-associated pneumonia, wound sepsis, endocarditis, meningitis, and urinary tract infections. Moreover, over the last 30 years, some strains acquired resistance to several antimicrobial drugs. They are currently known as Multi-Drug Resistant (MDR) *A. baumannii*. These strains quickly disseminated in many healthcare settings worldwide becoming an important nosocomial threat[43]. Several investigations have reported that MDR *A. baumannii* infections in different regions of the world including Europe, North America, Argentina, Brazil, China, Taiwan, Hong Kong, Japan, and Korea are often associated with nosocomial infections[44-48]. *A. baumannii*, like other important nosocomial pathogens, is able to survive on dry surfaces under hard conditions, as lack of nutrients, and this facilitates their persistence and transmission[21]. A study showed that *A. baumannii* is more resistant than *Escherichia coli* on dry surfaces, where it is able to persist for more than 4 months. In addition, it can survive for more than 20 days

on glass surfaces while placed at room temperature[49]. For these reasons, colonized medical devices and equipment represent an important reservoir in prolonged hospital outbreaks. Contamination of hospital environment and equipment with *Acinetobacter* spp outbreaks has indeed been often reported. A lot of colonized objects or materials likely to carry the micro-organism have been identified. These include pillows, bed linen, curtains, bedrails, bedside tables, water used for nasogastric feeding or ventilator rinsing, gas taps behind the beds, door handles, computer keyboards, sinks, and/or even cleaning and respiratory equipment used for mechanical ventilation, suctioning, devices related to intravascular access[50-53]. Also, HCWs' hands can be colonized with *A. baumannii*, thus promoting the transmission to patients[52]. Epidemiological studies showed that nurses and physicians had a colonization rate of the hands ranging between 3% and 23% and that the colonization was often temporary, excluding the case of injured skin[54,55]. *A. baumannii* is one of the principal causes of nosocomial pneumonia even if it is very difficult to differentiate between simple colonization and a real pneumonia[56]. The frequency of nosocomial pneumonia in ICUs is 3-5% with a crude death rate of 30-75%[57]. *A. baumannii* causes 1.3% of all the nosocomial bloodstream infections (BSI) (0.6 BSI/10,000 admissions), especially for the ICU-acquired forms (when compared to non-ICU) and are frequently caused by intravascular and respiratory tract catheters[54,58]. However, the origin of the bacteremia remains unclear in about 21-70% of the cases[54]. Previous reports showed that the death rate from *A. baumannii* BSI is variable from 34% to 43% at ICU and 16% in other wards[58,59]. Many studies have shown the importance of environmental cleaning in controlling outbreaks of MDR *Acinetobacter* spp. in critical care units[8,60,61]. Particularly, some scholars showed the success of a cleaning program based on the use of sodium hypochlorite in the management of outbreaks, along with hand hygiene program, patient surveillance, barrier precautions, contact isolation, cohorting affected patients[62,63]. During an outbreak of Carbapenem-resistant *A. baumannii,* Doidge et al[64] found that performing the cleaning with a commercial oxidizing disinfectant containing 50% potassium peroxomonosulfate, 15% sodium alkyl benzene sulfonate, and 5% sulfamic acid instead of normal detergent and alcohol wipes could rapidly lead to the conclusion of the outbreak.

Carbapenem-Resistant Enterobacteriaceae (CRE)

Over the last years, *carbapenem-resistant Enterobacteriaceae* (CRE) have become an important cause of HAIs worldwide. Outbreaks have been reported from different countries including the USA[65-70]. The resistance to carbapenems have been found in many Gram-negative species, including both *Enterobacteriaceae* (e.g., *Escherichia coli*, *Enterobacter* spp, *Serratia* spp) and non-fermenters (e.g., *Pseudomonas aeruginosa* and *Acinetobacter baumannii*), but *K. pneumoniae* is the most frequent species. Carbapenemase-producing *K. pneumoniae* is a nosocomial pathogen especially causing HAIs such as urinary tract infections, septicemia, pneumonia and intra-abdominal infections, but it is not commonly responsible for community-acquired infections[71,72]. Recent investigations[73-75] showed the role of hospital environment cleaning in the control of MDR coliforms transmission. Moreover, Kramer et al[21] demonstrated that *E. coli* and *Klebsiella* spp. are able to survive desiccation for more than a year, and *Serratia marcescens* for several months. Additional works[76-79] focused their attention on the resistance of MDR coliforms in a variety of health care environments, with evidence that MDR *Klebsiella* spp is found from surfaces more often than MDR *E. coli*. Several rechearches have been conducted to evaluate the presence of MDR CRE in the hospital environment. Lerner et al[79] showed the contamination of the hospital environment nearby KPC-producing CRE carriers and it found CRE around 88% of these patients. Fourteen sites were tested: bed linen around the head, crotch, and legs, personal bedside table, infusion pump, personal chair, dedicated stethoscope, an electrical outlet line, suction machine, respirator, cardiovascular monitor screen, pulse oximeter, manual respirator bag and enteral feeding pump. CRE were found on sheet surfaces nearby the pillow, inguinal area and legs, personal bedside table and infusion pump, but the detection rate of environmental CRE was inversely proportional to the distance from the carrier, being the bed surfaces the most contaminated sites[79]. Judge et al[80] screened highly touched surfaces located near carriers of MDR coliforms (light switch, bed rail, bedside locker, and mattress cover) and two sites situated in bathrooms common among patients (shower handrails and sink faucets). The results showed that MDR *K. pneumoniae* contaminated four sites either near

the patient or from the adjacent bathroom. The isolated environmental strains were the same as those isolated from the patient's urine. Other authors[81-85] demonstrated that hospital sinks represent one of the most frequent reservoirs for MDR Gram-negative bacilli, including MDR coliforms. In some cases, the replacement of the sink and related pipes and the improvement of the practices for sink usage and decontamination ended the outbreak. Many studies have highlighted the importance of hospital cleaning in the prevention of CRE infections. A 1995 report already emphasized this issue. Soulier et al[86] carried out an educational intervention to improve environmental cleaning and hand hygiene in an 11-bed gastrointestinal surgical ICU. The reported that performing the cleaning with glutaraldehyde along with the introduction of single-use equipment, barrier precautions and hand hygiene, decreased the rate of patients colonized with MDR *Enterobacteriaceae* from 70% to 40%[86]. Virgincar et al[87] emphasized the usefulness of additional chlorine-based cleaning following isolation of a CRE *K. pneumoniae* from patients in a United Kingdom hospital in eradicating the strain. This action was part of an infection control strategy including a urinary catheter care bundle, improved hand hygiene and contact precautions for all cases[87]. A very recent Italian study investigated the importance of enhanced cleaning in the reducing CRE infections. The program consisted of screening for CRE colonization through rectal swab cultures carried out in all patients admitted to high-risk units (ICUs, transplantation and hematology) or for any patients present in the same room occupied by CRE-positive patients in other units; grouping carriers, who have to be managed with strict contact precautions; enhanced education, cleaning and hand-washing programs; promotion of an antibiotic stewardship program. The authors reported that after the intervention, the incidence rate of CRE BSI and CRE colonization significantly declined over a period of 30 months.

Pseudomonas Aeruginosa

In the last decades, *Pseudomonas aeruginosa* has become a significant cause of HAIs[89], difficult to treat due to the limited antimicrobial susceptibility[90]. *P. aeruginosa* is one of the major pathogens causing ventilator-associated pneumonia, burn wound infections and nosocomial bacteremia, with an associated mortality rate >30%[91,92]. In the UK, *Pseudomonas* spp. causes ~4% of bacteremia representing the seventh most frequent cause, with an incidence of 7.3 per 100,000 population[93]. Many studies highlighted the importance of the healthcare environment as a reservoir of Pseudomonas spp., particularly of the hospital water systems that would represent the major contributors to *P. aeruginosa* transmission[93,94-98]. This pathogen is able to colonize and proliferate in the hospital environment even in relatively nutrient-poor conditions adapting to a wide range of temperatures. The importance of water systems in the *Pseudomonas* transmission has been known for a long time. A 1996 study showed that *P. aeruginosa* can be transmitted from contaminated sinks to hands during hand washing[99]. Moreover, some studies highlighted that strains of *Pseudomonas* isolated from water sources and adjacent surfaces are indistinguishable with those isolated from patient specimens[100,101]. An important role in *Pseudomonas* transmission is played by adherent biofilm that bacteria form on the surfaces of sinks, sink traps, pipes, water lines and hospital drains and that represents a persistent reservoir of this microorganism[102]. Biofilm protects bacteria from adverse environmental conditions and it prolongs the bacterial survival[103]. Particularly, in the context of biofilm, bacteria are more likely to resist chlorine-containing and other types of disinfectants and they demonstrate an increased antimicrobial resistance[104,105]. *P. aeruginosa* is an aerobic bacterium, and it thrives especially in the distal parts of the water distribution system, such as taps and sinks where the amount of oxygen is higher than the other parts[106]. For these reasons, rigorous and repeated cleaning strategies are necessary to disrupt the biofilm adherent in the internal walls of colonized water systems even if a total eradication is hardly realized[105]. Recently, Costa et al[107] showed the importance of hospital water in the transmission of *P. aeruginosa*. They considered ten patients with acquired nosocomial infection to *P. aeruginosa* in an ear, nose and throat department. After environmental and clinical sampling, they found a *P. aeruginosa* contamination in the water deriving from a drinking water fountain. Comparing the isolates, they found that the clinical had indistinguishable random amplified polymorphic DNA profiles from those environmental isolated from three patients. The contaminated water was used for the patients' alimentation and was the origin of the outbreak[107].

Gram-Positive Bacteria

Methicillin-resistant Staphylococcus aureus (MRSA)

In 1997, Boyce et al[108] published a study showing the presence of MRSA in the near-patient surfaces and the subsequent possibility for HCWs to contaminate their hands and gloves touching these surfaces. Afterward, several studies have shown the diffusion of nosocomial MRSA[109,110] and the importance of hospital cleaning to reduce hospital surfaces MRSA-contamination and MRSA-outbreaks. A prospective controlled crossover trial was conducted in 2009 into two acute-care surgical wards. The results showed a higher rate of MRSA acquisition when routine cleaning was carried out, while there was a decreased of more than half of cases during the period of enhanced cleaning. This report showed that the cleaning of at-risk sites, such as hand-touched surfaces, is able to reduce the risk of MRSA infection[111]. In 2011, Datta et al[112] highlighted the importance of enhanced cleaning in the acquisition of MRSA and VRE in rooms previously occupied by patients colonized by these pathogens. Acquisition of MRSA decreased from 3% to 1.5% and from 3% to 2.2% for VRE, showing that enhanced cleaning may reduce MRSA and VRE transmission. Finally, two recent works focused their attention on the efficacy of an enhanced cleaning carried out by two innovative sanitation methods in MRSA environmental contamination. The first study used a pulsed xenon UV device within a bundle comprising screening of patients, environmental sampling, hand hygiene and laboratory methods. This method reduced the rate of hospital-acquired MRSA acquisition by 56% after 6 months[113]. The second study was more protracted than the first and evaluated the efficacy of hydrogen peroxide (HP) decontamination along with patient screening for MRSA for a 6 years period. The HP decontamination was compared to the normal detergent cleaning in rooms previously occupied by MRSA carriers. MRSA was isolated from 25% of rooms cleaned with normal detergent and from 19% of rooms after use of hydrogen peroxide. Moreover, over the 6 years there was a reduction of the incidence of MRSA acquisition from 9 to 5.3/10,000 patient-days passing from detergent to disinfectant respectively[114]. Watson et al[115] evaluated the impact of implementing a hospital-wide environmental and patient cleaning protocol on the rate of MRSA infection and the cost-benefit of the intervention comprising an enhanced environmental cleaning of high touch surfaces, daily washing of patients with benzalkonium chloride and the isolation of patients with active infection. The MRSA rates decreased from 3.04 to 0.11/1,000 and the cost saving was estimated at $1,655,143.

Vancomycin-Resistant Enterococci (VRE)

The problem of VRE is well known across the world. Resistance to vancomycin in enterococci was first recognized in 1986, about thirty years after the introduction of this antibiotic[116]. Since then, there has been a progressive increase in the prevalence of this resistance microorganism, with the highest rates observed in the US. VREs are about one-third of *Enterococcus* isolates, causing 1,300 deaths each year[117]. Moreover, it has been demonstrated the prolonged survival of these pathogens in the hospital environment[21] and their resistance to normal cleaning practices, also using powerful disinfectants as a bleach-based cleaning[118-120]. Many Authors[10,118] showed that these pathogens remain on surfaces after an inappropriate cleaning, e.g., after a short action time of disinfectant or when surfaces are simply cleaned but not deeply rubbed. This can be the cause of the increased risk of VRE acquisition for patients placed in a room previously occupied by an individual colonized or infected with VRE[121]. However, Ford et al[122] showed that a previous VRE-colonized room occupant would not increase risk because, using a VRE molecular strain typing, isolates from 20 patients compared with those isolated from prior occupants were indistinguishable in only one pair. Some scholars showed the efficacy of an enhanced cleaning on the surface contamination and the patient acquisition of VRE, alone and in association with a hand hygiene program and/or other conditions[123-125]. Recent studies highlighted the importance of hospital sanitation in VRE control. In 2012, two different studies were carried out in Brazil and Australia as a response to increasing numbers of patients with VRE. In the first one, a set of activities including an enhanced cleaning, contact precautions and the introduction of an educational program was realized. This action led to a significant reduction in the acquisition rate from 1.49 to 0.33[126]. In the second study, an analog protocol consisting of an enhanced surfaces cleaning and a hand hygiene program was carried out. After this control measures, the number of new patients colonized with VRE decreased of 24.8% while the environmental contamination decreased by

66.4%[127]. Investigators focused their attention on *Enterococcus hirae* nosocomial infection. This microorganism is considered to cause 1-3% of the *Enterococcus* spp. infections detected in clinical practice and to have an emerging role of the source of serious illness such as of endocarditis, acute pancreatitis, pyelonephritis, and septic shock[128-130].

Clostridium Difficile

Clostridium difficile infection (CDI) is an important cause of hospital-associated gastrointestinal disease in several health-care system[131]. Overall, 94% of CDI cases are related to healthcare with 29,000 deaths and $4.8 billion in excess healthcare costs[132]. Some researches have shown that patients with undiagnosed cases of CDI can come in healthcare facilities or are transferred from another spreading the microorganism especially via HCWs' hands[16]. The incidence of CDI is higher in females, whites and people >65 years old[132]. Healthcare facilities represent one of the most important places of *C. difficile* spores' transmission with many large outbreaks in several hospital settings[133-136]. It has been known for a long time that the primary reservoirs of *C. difficile* in hospitals and healthcare facilities are colonized or infected patients. Studies have shown a 20% to 40% rate of colonization in hospitalized adults compared with 2% to 3% in healthy adults[137]. The duration of hospital stay is a critical risk factor for the acquisition of the organism. Chalmers et al[138] showed that the reduction of the length of stay in hospitals plays an important role in the prevention of CDI[138].

The spores, deriving from inpatients stools, easily contaminate the hospital environment through the HCWs' hands and medical equipment and then they can be transferred to other patients by ingestion[139]. Airborne spread of *C. difficile* has also been reported[140]. For these reasons, frequent hand washing by healthcare personnel, cleaning and disinfection of the patient's environment have great importance in preventing CDI transmission. However, the spores are able to survive in the environment for months and they resist the general cleaning and disinfection measures especially those using alcohol-based products[141]. The organism was found around toilets and on floor surfaces, bedding, furniture, telephones and medical equipment[142,143]. Additional evidence suggesting an important role for the inanimate environment may be found in the observation that there is a greater risk of infection occurring in roommates or in those who are admitted to a room previously occupied by a patient with *C. difficile*[22].

The recommended products for environmental surfaces disinfection in rooms of patients with CDI are hypochlorite-based disinfectants because they are sporicidal at 1000 ppm. Several works[144,145] reported that chlorine-based agents are able to reduce environmental contamination by *C. difficile* and consequently to decrease CDI incidence. Moreover, due to the importance of HCWs' hands contamination in the transmission of *C. difficile* spores, many studies have been conducted to verify the efficacy of various products. These reports[146,147] demonstrated that hand washing with soap and water, or with an antimicrobial soap and water, are more effective at removing *C. difficile* spores than alcohol-based hand hygiene products.

Conclusions

The role of the hospital environment in the transmission of HAIs is still debated worldwide. However, scientific evidence supports the hypothesis that hospital can act as an important reservoir of many nosocomial pathogens in several environments such as surfaces, medical equipment and water system. Healthcare settings are complex realities within which there are many critical points. Microbial contamination can result from the same inpatients, relatives and healthcare workers. Moreover, the use often inappropriate of antibiotic therapies causes the selection of multi-drug resistant pathogens that thrive and spread within the structure. Finally, the sometimes-incorrect behavior of healthcare workers can determine the cross-transmission of pathogens by environment-patients and patient-to-patient routes. An adequate and routine cleaning of the hospital environment, antimicrobial stewardship and educational campaign about correct behaviors to adopt by healthcare workers can represent possible solutions to this problem. Innovative sanitation methods are in the work, among which the use of probiotic bacteria in preventing the environmental contamination of hospital surfaces by pathogens[148,149].

Conflict of Interest
The Authors declare that they have no conflict of interests.

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