Gadi Borkow *Editor*

Use of Biocidal Surfaces for Reduction of Healthcare Acquired Infections

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Preface

Gadi Borkow

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Healthcare-acquired infections (HAI) have become a very significant medical concern both in developed and in developing countries, especially as microorganisms have developed high resistance to the existent antibiotics arsenal. While no exact numbers exist, it is assessed that millions of people worldwide acquire a HAI each year. These infections contribute significantly to morbidity, mortality and hospitalization costs. For example, in the United States alone, it was estimated that ~2 million HAI occur each year by all types of microorganisms, causing or contributing to ~100,000 deaths and adding ~$10 billion in additional healthcare expenses annually [1–3].

In order to reduce HAI rates, the medical community has developed aggressive measures – such as use of disposable equipment, healthcare staff education for improved hygiene, increased number of nurses and infection control personnel, isolation of infected patients, better ventilation management, use of high-efficiency particulate air filters, improved disinfection regimens, and use of aggressive antibiotic control programs. Indeed, all these measures have resulted in significantly lower HAI rates; however, even in hospitals where these infection control measures are rigorously implemented, the HAI rates are still unacceptably high, and it is clear that the current modalities to eliminate HAIs are not sufficient. The risk of an individual to acquire an infection while in the hospital is still intolerable and additional ways to fight HAI need to be developed (Fig. 1.1).

There is increasing evidence that potentially overlooked and neglected sources of nosocomial pathogens that significantly contribute to HAI are contaminated non-intrusive soft and hard surfaces located in the clinical surroundings, and that

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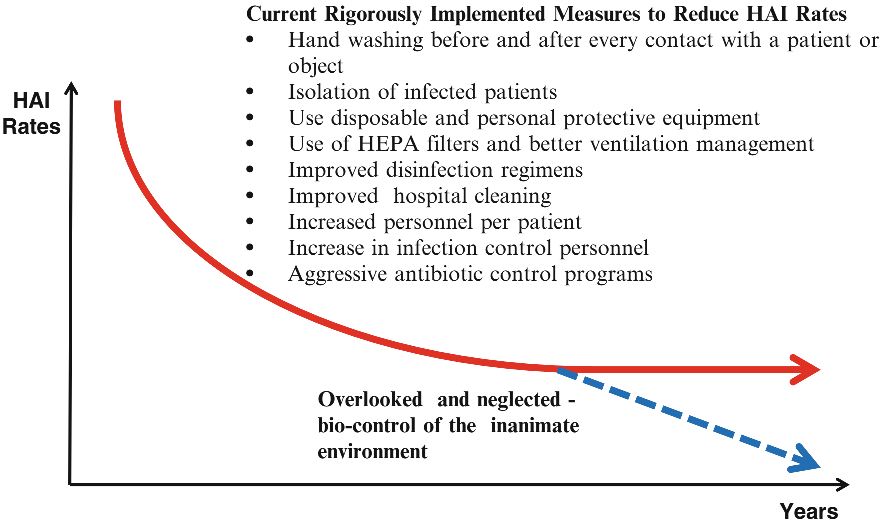

Fig. 1.1 HAI are not eliminated by the current implemented measures

there is a clear correlation between the environmental bioburden present in a clinical setting and the risk of patient of acquiring an infection [4–14]. Thus using self-disinfecting surfaces can be a very important adjunct in the fight against HAI [15, 16].

Copper is an essential trace element needed for the normal function of all aerobic life forms. Its ability to cycle between two oxidation states, Cu^{1+} and Cu^{2+}, is key to a wide array of metalloenzymes that catalyze electron transfer reactions. Conversely, copper can be highly toxic due in part to its ability to generate reactive oxygen species. Thus microorganisms have developed a complex series of mechanisms to regulate copper intracellular accumulation and distribution [17, 18]. However, above a certain threshold of exposure to copper, which varies between microorganisms, the microorganisms are killed, sometimes within minutes (e.g. [19–21]), via different multisite parallel mechanisms [22].

The ancient Greeks in the time of Hippocrates (400 BC) were the first to discover the sanitizing power of copper. They prescribed copper for pulmonary diseases and for purifying drinking water. Since then copper has been used as a biocide for treating sores and skin diseases and for purifying water by many civilizations, such as the Celts, Phoenicians, Egyptians, Hindus, and Aztecs [23]. By the eighteenth century copper had come into wide clinical use in the Western world for the treatment of mental disorders and afflictions of the lungs. Furthermore, in the eighteenth century it was discovered that no fungi grew on seed grains soaked in copper sulphate. Beginning in the early 1950s [e.g. [24–26]], the biocidal properties of copper and copper compounds were demonstrated in controlled laboratory studies. Notably, copper surfaces or copper compounds have been shown to be efficacious against hard-to-kill spores [27–33].

Today copper biocides have become indispensable and many thousands of tons are used annually all over the world for (i) prevention of roof moss formation [34];

(ii) wood preservation [35]; (iii) control of green slime in farm ponds, rice fields, irrigation and drainage canals, rivers, lakes and swimming pools [36]; (iv) prevention of downy mildew on grapes [37]; and (v) antifouling paints [38–40].

Non-soluble copper compounds, such as degradable phosphate glass fibres impregnated with CuO [41, 42], glass coated with thin films of CuO [43], or metallic and copper alloys [20, 32, 44–50] also exert potent biocidal properties, including against hard-to-kill spores [27–33]. Importantly, in March 2008 the U.S. Environmental Protection Agency (EPA) has approved the registration of copper alloys as materials with antimicrobial properties, thus allowing the Copper Development Association (CDA) to make public health claims [51]. More recently, Cupron Inc. received similar approvals by the EPA to make public health claims with its copper oxide infused countertops. These public health claims acknowledge that alloys containing above 60 % copper and surfaces impregnated with 16 % copper oxide particles are capable of killing more than 99.9 % of harmful, potentially deadly bacteria, such as Methicillin-resistant *S. aureus* (MRSA) within 2 h, and continue to kill more than 99 % of bacteria even after repeated contamination. Copper is the only metal that has received this type of EPA registrations.

This book discusses the role of the environment as a potential source for outbreaks of HAI and focuses on the utility of solid copper surfaces and copper oxide impregnated materials in reducing bioburden and fighting HAI. It also reviews other biocidal surface alternatives and the economics of using biocidal surfaces in a hospital environment. Finally, it discusses the pros and cons of existent disinfection modalities other than biocidal surfaces.

More specifically, in Chap. 2 of this book, Axel Kramer and Ojan Assadian, discuss the ability of pathogenic bacteria, fungi and viruses to persist and survive for long-term periods on inanimate surfaces. They discuss the factors influencing the survival of these pathogens in the environment and the mechanisms by which pathogens are transmitted from these inanimate surfaces to susceptible patients.

In Chap. 3, Jon Otter, Saber Yezli and Gary L. French provide proof that surface contamination by nosocomial pathogens shed by patients contributes to nosocomial cross-transmission and HAI. They review evidence that improved environmental hygiene can help bring HAI rates down and consider various options to address contaminated surfaces in healthcare facilities.

In Chap. 4, Michael G. Schmidt, Andrea L. Banks, and Cassandra D. Salgado, further discuss the effect of environmental contamination and HAI and review the studies showing the use of biocidal metallic copper surfaces resulting in dramatic reduction of bioburden and importantly of HAI rates.

In Chap. 5, I discuss how regular hospital linens, uniforms and other hospital textiles are a neglected source of nosocomial pathogens and how self-disinfecting biocidal textiles can significantly contribute to the reduction of HAI. Specifically I review the studies showing that incorporation of copper oxide in hospital textiles can reduce bioburden and HAI rates. I also briefly review the novel successful endowment of biocidal properties to non-porous solid surfaces by impregnating them with copper oxide particles.

In Chap. 6, Christophe Espírito Santo, Nadezhda German, Jutta Elguindi, Gregor Grass, and Christopher Rensing, discuss why on the one hand copper is an essential element to microorganisms and how copper homeostasis is achieved, and on the other hand how copper exerts its potent biocidal properties, with special focus on the molecular mechanisms underlying bactericidal properties of solid copper surfaces.

In Chap. 7, Jon Otter reviews potential and existent biocidal surface alternatives to copper. He discusses what should be the ideal biocidal surface candidate and discusses the pros and cons of each of the existent candidate alternatives, the optimal deployment modes, the surfaces that should be made self-disinfecting surfaces, and how do we test and compare efficacy of antimicrobial surfaces.

In Chap. 8, Panos A. Efstathiou evaluates the impact of using biocidal surfaces in a hospital environment, specifically discussing the use of metallic copper surfaces in the intensive care units, reaching the conclusion that the use of biocidal surfaces has significant positive economic advantages.

Finally, in Chap. 9, George Byrns reviews the pros and cons of using chemical fumigation and germicidal UVC irradiation in healthcare and other related settings. He raises the concern that while both fumigation and UV irradiation are capable of killing microorganisms, it is uncertain whether the benefits in terms of overall hospital patient infection rates outweigh the risks and costs associated with these methods, further strengthening the importance of using biocidal self-disinfecting surfaces to combat environmental contamination.

I hope this book will give significant support to the notion that the inclusion in clinical settings of self-disinfecting biocidal hard and soft surfaces can significantly help in the fight against healthcare-acquired infections. I also hope you will find this book informative, comprehensive and interesting.

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Chapter 2
Survival of Microorganisms on Inanimate Surfaces

Axel Kramer and Ojan Assadian

Contents

Abstract In healthcare settings microbial contaminated surfaces play an important role in indirect transmission of infection. Especially surfaces close to the patients' environment may be touched at high frequencies, allowing transmission from animated sources to others via contaminated inanimate surfaces.

Therefore, the knowledge on the survival of bacteria, fungi, viruses and protozoa on surfaces, and hence, in a broader sense, in the human environment, is important for implementing tactics for prevention of Healthcare-acquired Infections (HAI).

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This chapter will elaborate the role of surfaces in the transmission of pathogens. Particular emphasis is laid on the current knowledge of the survival time and conditions favouring survival of the pathogens. Finally, mechanisms of transmission from inanimate surfaces to patients are highlighted.

Within the multi-barrier strategy of the prevention of HAI, environmental disinfection policies should be based on risk assessments for surfaces with different risks for cross contamination such as high- and low-touched surfaces with appropriate standards for adequate disinfection measures under consideration of the persistence and infectious dose of the pathogens. As a result, surface disinfection is indicated in the following situations:

- Frequently touched surfaces adjacent to patients
- Surfaces with assumed or visible contamination
- Terminal disinfection in rooms or areas where infected or colonized patients with easily transferable nosocomial pathogens are cared for, and
- in outbreak situations.

Furthermore, the knowledge of the persistence of pathogens will also support ensuring the biosafety in microbiological and biomedical laboratories, food-handling settings, and for hygienic behaviour in the everyday life to prevent transmission of infectious diseases.

Keywords Persistence • Bacteria • Fungi • Viruses • Protozoa transmission mechanisms • Surface disinfection

List of Abbreviations

HAI	Healthcare-acquired infections
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	Methicillin-sensible *Staphylococcus aureus*
RH	Relative humidity
SARS	Severe acute respiratory syndrome
VRE	Vancomycin-resistant enterococci

2.1 Introduction

Microorganisms may be transmitted from animated sources to inanimate environmental sources, which may become secondary reservoirs if they meet the needs of transmitted pathogens to survive and to multiply. In healthcare settings, however, contaminated surfaces, which may not always be optimal for microbial survival and multiplication, still may play a role in the chain of infection, since surfaces close to the patients' environment may be touched at high frequencies, allowing transmission from animated sources to others via contaminated inanimate surfaces.

Because of this, the knowledge on the survival of bacteria, fungi, viruses and protozoa on surfaces, and hence, in a broader sense, in the human environment, is important for planning and implementing tactics for prevention of Healthcare-acquired Infections (HAI). Furthermore, such knowledge will also assist ensuring the biosafety in microbiological and biomedical laboratories, food-handling settings, and for hygienic behaviour in the everyday life to prevent transmission of infectious diseases.

One example of microorganisms with relatively short ability of persisting in the environment is the severe acute respiratory syndrome (SARS) coronavirus (CoV), which became pandemic within months in China in 2002. This virus retains infectivity on different substrates up to 9 days, as compared to the influenza virus, which demonstrates a relatively long persistence in the environment up to 4 weeks [112]. Both viruses are airborne transmitted infectious agents, however, they may also be transmitted via hand-surface contacts, supporting the relevance of hand hygiene and personal protection against infection.

Because of a number of microorganisms' ability to persist and survive for long-term periods on surfaces, particularly in healthcare settings, the usage of antimicrobially impregnated surfaces is increasingly discussed [82]. However, because of the required long contact times of microorganisms on antimicrobial surfaces [64, 65, 25, 45], such technologies may be useful for surfaces with low frequency of hand contacts.

2.2 The Role of Surfaces in the Transmission of Pathogenic Microorganisms Causing Healthcare-Acquired Infections (HAI)

In healthcare settings, bacteria, bacterial spores, viruses and yeasts are mainly transmitted from infected and/or colonized patients, but also from staff, and in some situations from visitors to the inanimate hospital environment, particularly to areas adjacent to patients and frequently touched surfaces by hands ("high-touch surfaces"). Potential pathogenic microbial flora of the respiratory tract and of the vestibulum nasi, such as methicillin- sensible (MSSA) or resistant *Staphylococcus aureus* (MRSA), is correlated with a higher risk of contamination of surrounding surfaces through direct or indirect contact with hands [81]. Intestinal infections caused i.e. by *Clostridium difficile* and Norovirus, or enteral colonization with nosocomial pathogens such as vancomycin-resistant enterococci (VRE) may also be associated with a risk of widespread environmental contamination [30]. Compared with the large number of published literature on environmental contamination with MRSA, VRE, and *C. difficile*, there are relatively few published studies on environmental contamination by Gram-negative bacteria [64, 65]. Aside of a possible publication bias in the past, one reason for this is the different ability of Gram-positive and Gram-negative bacteria to survive in the inanimate environment.

The level of microbial bio-burden on surface in healthcare settings is low compared to the numbers on patients' skin or in faeces. However, even at low particle numbers