Probiotic-Based Sanitation in the Built Environment

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The use of conventional chemical disinfectants is a common practice in built environments and has drastically increased in response to the COVID-19 pandemic. While effective for instantaneous disinfection, the application of chemical disinfectants to indoor surfaces is associated with recontamination and is prone to select for antimicrobial-resistant pathogens. In contrast, probiotic-based sanitation (PBS) relies on the premise that probiotic bacteria, namely apathogenic *Bacillus* spp., when combined with eco-friendly detergents and applied to indoor surfaces can outcompete and exclude pathogens.

disinfectant | probiotic-based sanitation | antimicrobial resistance | COVID-19 | microbiome | built environment | *Bacillus*

1. Introduction

The use of chemical disinfectants is a common practice in our built environments (BE), including homes, workplaces, schools, industries, public transportation, healthcare clinics and hospitals. While hundreds of different antimicrobial chemicals are used as the active ingredients in disinfectants, the most common antimicrobial chemical groups include quaternary ammonium compounds (QAC), chlorine and chlorine compounds, alcohols and phenols [1][2]. In 2020, the Environmental Protection Agency (EPA) released its initial List N: Disinfectants for Use Against SARS-CoV-2, which now contains over 500 chemical disinfectant products that meet the EPA's criteria for use against SARS-CoV-2 [3]. The production and consumer use of these chemical disinfectants rose drastically during the COVID-19 pandemic and is predicted to substantially increase over the next decade [4].

While effective and consistent sanitation practices are essential to protect individual and public health, conventional chemical-based disinfection has several notable limitations that are directly and indirectly associated with adverse human health effects. Chemical disinfectants are time dependent and are often only effective on cleaned surfaces for minutes to hours after proper application; therefore, these products are generally not effective against recontamination [5][6]. Persistent recontamination is a leading cause of hospital acquired infections (HAIs), and contributes significantly to the spread of infection within childcare centers and households [7][8][9]. Additionally, recent studies have identified chemical disinfectants as a leading cause of bacterial resistance to disinfectants and cross-resistance to antibiotics [10][11][12]. The effective dose of any biocide depends on the formulation, the type of surfaces treated, temperature and contact time [13][14]. Prolonged exposure to sublethal concentrations of chemical disinfectants can select for tolerant organisms, and therefore simultaneously increase the abundance of antimicrobial-resistant genes and antibiotic-resistant organisms [15]. In fact, the environments with the highest levels of disinfectant use also harbor the highest rates of multi-drug-resistant microbes [16][17]. Nearly 10% of bacterial samples isolated from local indoor fitness centers frequently disinfected with QAC-containing products were found to be resistant to in-use disinfectant concentrations and the majority of QAC-resistant strains were also resistant to ampicillin, erythromycin, penicillin, ciprofloxacin and chloramphenicol [18]. Survival of QAC-tolerant MRSA on automated teller machines was suggested to be facilitated by low disinfectant concentrations [19], and numerous outbreaks have been documented and attributed to disinfectant-resistant pathogens that have contaminated antiseptic products [20][21][22][23]. Antimicrobial resistance has been declared as one of the top ten global public health threats that require urgent multisectoral action [24].

The prolific and unprecedented use of chemical disinfectants during the COVID-19 pandemic has also led to a rise in acute exposure incidents [25][26][27][28]. Consistent with public health recommendations for increased cleaning, 2020 survey results indicate that more than 70% of households increased the frequency of disinfection during the COVID-19 pandemic, and 80% of the households reported routinely using chemical disinfectant products [29]. Unfortunately, more than one third of households use chemical disinfectants unsafely [30][31]. Comparing data from the US National Poison Data System from January through March of 2019 and 2020, National Poison Control Centers received a 20.4% increase in calls related to disinfectant exposures in 2020 [25]. Similar data have been reported internationally [27][28]. Moreover, the frequent detection of QACs in blood, tissue and breastmilk confirms that human exposure to chemical disinfectants is significant and widespread [29][32][33]. Notably, QAC concentrations in blood samples taken in 2020 were correlated with biomarkers of inflammation, mitochondrial dysfunction and sterol imbalance [34]. Numerous case studies have suggested that acute exposure to chemical disinfectants can cause irritant and allergic contact dermatitis and contribute to the development of occupational asthma [35][36][37][38]. A multi-year study from 2009 to 2015 identified regular chemical disinfectant use by female nurses as a major risk factor for developing COPD [39]. Likewise, chlorine compounds from chlorine-based disinfectants have been known to react with organic materials in water to form toxic and corrosive disinfection by-products that are harmful to humans, animals, plants, ecosystems and built environments [40]. Several reviews have attempted to evaluate current consumer exposure to chemical disinfectants and associated health risks and have concluded that indoor chemical disinfectant use poses distinct human and environmental health threats [40][41][42][43]

2. Probiotic-Based Sanitation

Given the evidence, there is a pressing need for effective, safe and eco-friendly sanitation approaches as an alternative to chemical disinfectants. Along with the growing understanding of the importance of microbiome health, emerging evidence supports a bidirectional hygiene (“bygiene”) approach to sanitation that aims to target and reduce pathogen burden yet maintains the natural microbial biodiversity in the built environment—thus, limiting the risk of infection and promoting the survival of, and exposure to, beneficial microbes [44][45][46]. In contrast, the sole aim of disinfection is to eliminate pathogenic microorganisms on objects and surfaces [2]. In the process, chemical disinfectants offer a trade-off—eradicate the potential pathogen, but also destroy the resident microbes. A recent assessment of disinfectant versus plain soap sanitation approaches found that the use of chemical disinfectants strongly promoted the survival of pathogenic bacteria on cleaned surfaces [47]. Specifically, on surfaces cleaned with chemical disinfectants, pathogens outcompeted the resident microbes, but on surfaces cleaned with plain soap, resident microbes outcompeted the pathogens [47]. These results suggest that both maintaining microbial diversity and fostering an environment where apathogenic species can outcompete pathogens are critical components of effective sanitation systems.

This competitive exclusion principle is the basis for biocide-free, probiotic-based sanitation (PBS). The benefits of probiotics on human health have been increasingly touted for years [48][49][50]. Probiotics, defined as “living microorganisms that confer a benefit to the host when administered in adequate amounts” [48], have been widely accepted as safe and effective therapies to prevent and treat a wide range of human health problems including inflammatory bowel disease (IBD), antibiotic-resistant skin infections, gastrointestinal and urogenital bacterial infections, gingivitis and allergic disorders [51][52][53][54][55][56][57]. The mechanisms by which probiotics provide these human health benefits are still actively being investigated. The prevailing theory is that probiotic species, in adequate numbers, are able to outcompete pathogens for nutrients and space via a variety of microbial mechanisms (production of antimicrobial compounds, community interactions, quorum sensing, host immune system modulation, etc.); although the particular mechanisms of action and host effects are largely species- or even strain-specific [58].

Similar to individuals, built environments (BE) have microbiomes that are composed of microorganisms inhabiting surfaces and inanimate objects, and circulating in ventilated air [59][60]. BE microbiomes are generally composed of commensal microbes of human origin that colonize and persist in indoor environments. The composition of BE microbiomes is highly dynamic and is influenced by human and environmental factors including climate, temperature, sanitation practices, level of human occupancy and various other human activities [61]. Recent studies indicate BE microbiomes actively impact human and public health, acting as a potential reservoir for pathogens [62][63]. A global, 3-year, 60-city study that cataloged the microbiomes of mass-transit systems identified the presence of antimicrobial resistance (AMR) genes in the majority of sampled locations, although unevenly distributed [64]. Routine disinfectant use has been suggested to promote the survival and proliferation of antimicrobial-resistant microbes in BEs [63]. Accordingly, the idea that PBS could be used to effectively and sustainably modulate and protect BE microbiomes without the prolific use of chemical disinfectants has become an attractive, yet underacknowledged, sanitation strategy in recent years. This general PBS hypothesis was first proposed in 2009, with the aim of combating nosocomial infections by applying probiotics to frequently contaminated patient equipment [65]. Since then, eco-friendly detergents with high concentrations of apathogenic, food-grade bacterial spores of the *Bacillus* genus (namely *B. subtilis*, *B. pumilus* and *B. megaterium* species) have been the predominant PBS system investigated. *Bacillus* spores are effectively able to survive a wide range of temperatures and pH environments [66][67]. Once diluted and applied, *Bacillus* spores are able to germinate and quickly colonize dry inanimate surfaces, ultimately dominating the composition of the resident microbiome and competitively excluding pathogens from surviving and colonizing these high-touch surfaces [68].

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