

Combating Multi-Drug Resistant Organisms (MDROs) through an Innovative Soft-Surface Based Intervention

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Introduction

The rise of antibiotic-resistant microbes is a challenge on a global scale, impacting the lives of people on a daily basis. In the United States alone, at least two million people are infected annually with antibiotic-resistant microbes, resulting in at least 23,000 mortalities (1). To address this challenge, key organizations like the Centers for Disease Control and Prevention (CDC) are encouraging and investing in innovative strategies to enhance and strengthen current best practices and antibiotic stewardship programs (2). In this article, we discuss an innovative approach to address the spread of pathogens, including multidrug-resistant organisms (MDROs), through an innovative soft-surface infection prevention strategy applicable to healthcare and sports medicine infection control programs.

The growing emphasis on infection prevention

With the increasing appearance of antibiotic-resistant microbes, innovative preventative measures are gaining in importance as an effective and complementary approach to the development and administration of new antibiotics. These include improved ways to measure hand hygiene compliance (3), UV-based room disinfection (4), surface disinfection of immobile (5) and mobile hard surfaces (6), nasal decolonization (7) and CHG bathing (8), among others. Effective infection prevention programs must include prevention strategies that address all key modes of disease transmission within the patient environment. The need to address infection prevention using new approaches became that much more evident during COVID-19, when the impact of the lack of human resources due to time diversion was most felt (9). The impact of COVID-19 on traditional healthcare-associated infection prevention efforts demonstrates the effect of COVID-19 on personnel and resources. This further supports the need for infection prevention measures that can function independent of an infection preventionist (9).

The critical role of textiles and the environment in the spread of MDROs

Many studies have highlighted the fundamental role of soft surfaces and the environment in the spread of infections (10-14).

Shedding of pathogens as the human skin (epidermis) is continuously being renewed possess a significant infection prevention challenge from the soft surface point of view (14). This is particularly well-highlighted in several recent reports that uncover the role of the environment (including soft surfaces) in the spread of an emerging drug-resistant pathogen, *Candida auris*. Immunocompromised patients infected with *C. auris* shed large amounts of the pathogen through their skin onto surrounding environmental surfaces (including bed linens) that then serve to spread the infection (15). Similarly, in a study by Donskey et. al., 74% of methicillin-resistant *Staphylococcus aureus* (MRSA) carriers in a hospital and long-term care facility showed the presence of MRSA on clothing (16). In many cases, the environmental spread of MDROs is harder to trace, as patients may transmit them even when they are not actively infected. Residents in post-acute care facilities are a good example, where a high rate of prevalence and colonization is associated with the transmission of MDROs. In a recent study in Clinical Infectious Diseases (17), the authors found that the prevalence of MDROs was 65% in nursing homes (NHs) and 80% in long-term acute care facilities (LTACs). MDRO status was known for 18% of NH residents and 49% of LTAC patients. MDRO colonized adults commonly harbored additional MDROs (> 54% MDRO in NH residents and > 62% MDRO in LTAC patients).

Hospital privacy curtains represent another surface that gets easily and heavily contaminated, due to the frequent handling by healthcare workers and current changeout schedules of several weeks. A recent study showed that hospital privacy curtains are a breeding ground for MRSA, and by day 14 post-hanging, 87 % test positive for it (18). Das et.al. demonstrated that privacy curtains contaminated with carbapenemase-resistant *Acinetobacter* resulted in an outbreak (19). Another study on environmental reservoirs for MRSA found that over half the surface samples taken from beds and mattresses were positive for MRSA. This further supports the need for linens that have a residual antimicrobial activity against microorganisms (20).

Fungal outbreaks are often linked to contaminated textiles because of the ability of fungal spores to survive on textiles for extended periods of time. In a recent study conducted at 15 transplant and cancer hospitals, 33% of freshly laundered textiles were visibly unclean and *Mucorales* was identified on > 10% of the textiles (21).

The use of energy-efficient washing machines can also lead to a build-up and transmission of MDROs, as recently reported by Schmithausen et. al. In tracing the source of infections to newborns through knitted socks and hats at a German hospital, the authors identified the accumulation of extended-spectrum beta-lactamase (CTX-M-15)-producing *Klebsiella oxytoca* ST201 in the residual wash water, resulting in contamination of clothing during the laundry process (22). A temperature of at least 160°F (71°C) for a minimum of 25 minutes is commonly

recommended for hot water washing. Some non-industrial washers cannot achieve this high of a temperature.

Similar risks have been identified in athletic facilities where athletic gear and towels serve to transmit community-acquired pathogens such as MRSA (23-25).

Taken together, this growing body of evidence highlights a) microbial shedding by people onto textiles represents an important area of unaddressed risk and b) MDROs from carriers and infected people quickly contaminate the immediate surrounding environment.

These studies emphasize the need for implementation of measures to reduce soft surface contamination through active interventions as a means to reduce transmission of MDROs. Several studies have demonstrated that such approaches can indeed be effective in improving outcomes (26-28).

SilvaClean[®], an innovative silver ion-based intervention: technology and evidence

SilvaClean is an innovative approach that addresses the post-laundry contamination intervention gap for soft surfaces. The technology is based on silver ions, a well-known, natural antimicrobial form of silver (29-30).

The technology is delivered through a simple laundry process to enable soft surfaces with antimicrobial properties such that they actively participate in infection control through a residual antimicrobial effect. Installed at a laundry facility, the technology includes a smart dispensing device enabled by the cloud that doses Environmental Protection Agency (EPA) registered SilvaClean chemistry (31) onto all launderable textiles during the laundry rinse cycle through a quality-controlled process. The chemistry gets re-applied each time the textiles are laundered, maintaining the efficacy of the treated textiles. Because of its ability to be applied to all existing inventory (e.g., healthcare linens, scrubs, privacy curtains, towels, athletic gear, etc.), SilvaClean provides a cost-effective measure to incorporate a horizontal, soft surface intervention into an infection prevention program.

When SilvaClean chemistry is added to textiles during the laundering process, the silver ions bind to the textiles through a charge-based interaction. More importantly, the silver ions remain bound on the textiles throughout its use cycle, essentially converting existing textiles into actively antimicrobial textiles. The silver ions on the textiles are capable of residually killing pathogens, even as they become contaminated. This mode of action lends SilvaClean's antimicrobial benefits to address post-laundry contamination events, such as during use (e.g., microbial shedding from the patient or carrier skin onto linens or clothing), during handling (e.g., privacy curtains) and even in storage (e.g., freshly laundered and stored linens).

Through the following trimodal antimicrobial action of silver ions, SilvaClean provides an effective and complete kill against a wide range of microbes (29-30):

1) Cell lysis: Silver ions bind to the cell wall of the microbe, causing it to rupture.

2) Cell suffocation: Once inside the cell, silver ions attach to the metabolic enzymes, suffocating the cells.

3) Inhibition of DNA replication: The silver ions bind to strands of DNA to stop the replication process.

The residual efficacy of SilvaClean is complementary to routine laundry processes. These processes use a combination of heat and chemicals, such as chlorine, detergents, quaternary ammonium compounds and peroxide additives to reduce the microbial load from incoming dirty laundry. The action of these additives, while very effective in sanitizing textiles, is limited to the laundry cycle itself and provides a one-time kill.

SilvaClean chemistry was cleared to market by the EPA, making it the only residual, antimicrobial laundry additive with public health claims (31). Specifically, SilvaClean is approved to reduce post-laundry contamination with activity against *Staphylococcus aureus*, *Klebsiella pneumoniae*, MRSA, Vancomycin-resistant *Enterococcus* (VRE), ESBL-*Escherichia coli*, *Acinetobacter baumannii*, and *Candida albicans*. With this approval, the EPA acknowledges that pathogens can spread through textiles and that SilvaClean can be a useful and cost-effective addition to infection control programs.

Unlike resistance development with traditional antibiotics, resistance to silver involves a multitude of genes, and there are a limited set of studies that show resistance development from bacteria towards silver (32-33).

SilvaClean's utility in infection control programs is supported by multi-site studies. In one study, Openshaw et. al. (34) demonstrated that SilvaClean treated textiles show > 70% reduction in bioburden levels of *S. aureus* and > 80% reduction in the levels of MRSA on textiles contaminated due to microbial shedding from the patient. In the same study, the authors also showed that clean, stored textiles pick up contamination after delivery to the healthcare facilities and that the levels for both *S. aureus* and MRSA were reduced by > 90% when the textiles were treated with SilvaClean. This and other studies show conclusively that textiles serve as a conducive surface for the growth of microbes, including pathogens, and may potentially serve to propagate the contamination. Furthermore, the study showed that by providing an intervention through SilvaClean, the bioburden levels can be effectively reduced, with potential to contain the contamination. Additional early evaluations signify that SilvaClean-based reduction of *S. aureus* and MRSA bioburden on textiles results in a secondary reduction of their bioburden levels in the surrounding environmental surfaces that contaminated textiles come in contact with (unpublished data).

In another multi-year, multi-site clustered analysis study, Openshaw et. al. (35) evaluated the impact of SilvaClean inclusion in an infection control program on outcomes as monitored through healthcare-associated infection (HAI) rates. In this study, the addition of SilvaClean to

other standard interventions as an additional measure, resulted in a 43% reduction in HAI rates over an 18-month pre- and post-treatment retrospective analyses. Control sites that did not include SilvaClean to their standard interventions observed a 5% reduction in HAI rates during the same period, indicating that the inclusion of SilvaClean had a positive additive effect on the reduction of HAI rates. The HAIs that were monitored included *Clostridioides difficile* infections, central line-associated bloodstream infections (CLABSIs), catheter-associated urinary tract infections (CAUTIs), and surgical site infections (SSIs). When the analyses were extended to a 30-month pre- and post-treatment clustered retrospective analyses, the largest reductions were observed for *C. difficile* (50%) and CAUTIs (41%).

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Dr. Priya Balachandran, COO Applied Silver, is a microbiologist and infectious disease expert and has deep experience working with products and applications for infectious disease, molecular diagnostics, and public health. She is a successful researcher with peer-reviewed publications and patents and is an active member of the Association of Professionals in Infection Control and Epidemiology, the American Society for Microbiology, and the Infectious Disease Society of America. She obtained her Ph. in microbiology from the University of Alabama at Birmingham and did her postdoctoral fellowship in infectious disease and bacterial pathogenesis at the University of California, San Francisco.

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