Dry Hydrogen Peroxide: A Novel Solution for Reducing Microbial Bioburden in Healthcare

Executive Summary

Healthcare-associated infections (HAIs), and now COVID-19, place a huge burden on the U.S. healthcare system and the patients it serves. Collectively, HAIs cost American health facilities billions of dollars each year[1] as professionals working in hospitals and other healthcare settings attempt to prevent the spread of infection and treat the staggering number of patients who are sickened by infectious environmental pathogens. A growing number of these organisms are resistant to available antibiotic remedies. This increases the danger to affected patients - and the financial resources required to treat them. An estimated 72,000 patients die from HAIs annually and the number of patients succumbing to COVID-19 continues to climb daily, taking a devastating personal and financial toll on their loved ones.[2-3]

Research shows the reduction of bioburden mitigates the risk of infections.[4] While ongoing attempts have been made to reduce bioburden through improved manual cleaning and other sanitation initiatives, research shows that they have been largely ineffective, cumbersome and/or costly.[5]

Ineffective environmental cleaning and disinfection has critical implications, in terms of patient and healthcare worker safety,[6-9] patient satisfaction,[10] and institutional reputation.[10-11] Infections attributed to a dirty environment can also potentially lead to costly legal matters.[12]

Now, an innovative technology has emerged to support the efforts expended on environmental cleaning and disinfection. Synexis' dry hydrogen peroxide (DHP) technology is a microbial reduction system that provides a continuous and effective mechanism for reducing viruses, bacteria and mold in the air and on surfaces, as well as other infectious agents.[13-14] DHP has been effective in reducing bioburden in the food, hospitality, agriculture and animal health industries for the last 14 years and is now being used in a number of large healthcare systems across the country.

This technology, which invisibly delivers a gas composed of dry hydrogen molecules generated from a room's ambient humidity and oxygen, does not require ongoing behavior change or education of healthcare personnel. It is self-sustaining and allows continued microbial reduction while patient care areas remain occupied. This is in stark contrast to other "no-touch" methods, which can only be used for disinfection of a room after the patient has been discharged, otherwise known as terminal disinfection.

Research has shown that reductions in environmental bioburden not only produce better patient outcomes, but may also improve a facility's bottom line significantly. [15-16]

Introduction

Across the United States, healthcare-associated infections (HAIs) cost roughly 72,000 patients their lives each year in addition to leading to direct and indirect costs of $96-$147 billion annually.[1] According to the Centers for Disease Control and Prevention (CDC) – the nation's leader in tracking infections – HAIs are a significant cause of illness and death, and they "can have devastating effects on physical, mental/emotional, and financial health."[17]

An increasing number of HAIs are caused by "supergerms" or antibiotic-resistant organisms that effectively resist the antimicrobial drugs used to kill them.[17] A report from the CDC released in November 2019 conservatively estimated that infections developed due to antibiotic-resistant bacteria cause some 2.8 million Americans to become sick each year, and result in approximately 35,000 deaths.[18]

A large proportion of these infections can be attributed to inadequate or ineffective environmental cleaning that fails to prevent the transmission of infections among patients and caregivers.[19] While the effectiveness of different infection prevention methods has been rigorously studied, and a variety of cleaning and disinfection initiatives and approaches have been implemented for decades, infections have remained a persistent – and resistant – problem. Patients continue to be sickened by, and succumb to, infections such as catheter-associated urinary tract infection (CAUTI), central line-associated bloodstream infection (CLABSI), *Clostridioides difficile* infection (CDI), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococcus (VRE), and surgical site infection (SSI).

For healthcare administrators, this intractable issue has critical implications in terms of patient and employee safety, the damage to patient relations and institutional reputation, potential lawsuits, and the ongoing investment in environmental cleaning supplies and labor that – regardless of the diligence of those involved – is not having the desired effect.

The COVID-19 pandemic represents a serious global health threat that has taxed health systems across the world. [20-23]

In its most recent report on "Antibiotic Resistance Threats in the United States," released in November 2019, the CDC added two additional urgent threats: drug-resistant *Candida auris* and carbapenem- resistant *Acinetobacter*.[24] *Candida auris*, a fungus that has caused severe illness in hospitalized patients in several countries, can remain on environmental surfaces in healthcare settings for an extended period of time, leading to facility-wide outbreaks.[19] Carbapenem-resistant *Acinetobacter*, which resulted in 8,500 HAIs and an estimated 700 deaths in 2017, can cause pneumonia as well as wound, bloodstream and urinary tract infections.[24]

Clearly, more needs to be done to address the pernicious problem of reducing microbial bioburden which leads to infections – but what?

Background Environmental Contamination

Scientific literature has demonstrated that environmental contamination plays a significant role in the transmission of several key HAIs, including *Clostridoides difficile (C.difficile or C.diff)*, *Acinetobacter* spp., VRE, MRSA, and norovirus. Research shows that all of these pathogens can survive for hours, days, or even months, "to frequently contaminate the environmental surfaces in rooms of colonized or infected patients, to transiently colonize the hands of health care personnel, to be transmitted by health care personnel, and to cause outbreaks in which environmental transmission was deemed to play a role."[25]

Chart 1. Pathogen Survival Times

PATHOGEN	SURVIVAL TIME
S. aureus (including MRSA)	7 days to >12 months
Enterococcus spp. (including VRE)	5 days to >46 months
Acinetobacter spp.	3 days to 11 months
C. difficile (spores)	<5 months
Norovirus (and feline calicivirus)	8 hours >2 weeks
Pseudomonas aeruginosa	6 hours to 16 months
Klebsielle spp.	2 hours to >30 months
SARS-CoV-2	3 hours to 3 days

Adapted from Hota B, et al. Clin Infect Di. 2004;39:1182-9 and Kramer A, et al. BMC Infectious Diseases 2006;6:130 Adapted from Van Dormalen, et al. New Engl J Med 2020; 382: 1564-67.

These and other pathogens can contaminate virtually any surface in the room – bedding, overbed tables, phones, wash basins, privacy curtains, patient gowns, handrails, eating utensils, and more.

The air in a room has also been proven to be a vector for particulate matter, including harmful microorganisms. Studies have shown that after the toilet of a *C. diff* patient is flushed, for example, the bacteria can be recovered from the air around the toilet and may remain airborne for up to 90 minutes before falling and contaminating the surfaces in the room.[26] Meanwhile, new research demonstrates that the rooms of patients who are carrying *C. diff* but are asymptomatic are as contaminated as rooms of symptomatic patients.[27] Studies have also shown that a patient admitted to a hospital room that was previously occupied by a patient who was colonized or infected with MRSA, VRE, *Acinetobacter*, or *C. diff* is at higher risk of being infected or colonized with that pathogen.[25]

Environmental cleaning plays a critical role in preventing direct and indirect transmission of HAI-causing pathogens.[28] In an article that appeared in the journal *Antimicrobial Resistance and Infection Control,* author Dr. John M. Boyce said most experts can agree that "careful cleaning and/or disinfection of environmental surfaces, daily and at time of patient discharge, are essential elements

of effective infection prevention programs."[29] However, he went on to say that multiple studies have shown manual cleaning and disinfection of surfaces in hospitals to be "suboptimal."

Among the factors contributing to this dilemma are personnel-related issues. Although hand hygiene protocols are in place in the nation's healthcare facilities, many studies have shown that physicians and other providers often fail to follow those protocols. In fact, one recent study showed that just 32% of hospital physicians comply with accepted hand hygiene procedures before or after interacting with patients and touching potentially contaminated objects, and only 48% of nurses do.[30]

Research has revealed that even after manual cleaning, as many as 50% of surfaces remain contaminated with pathogens, including multidrug-resistant organisms (MDROs).[31]

Staff turnover represents part of the problem. More than 50% of hospitals reported staff shortages in their Environmental Services departments in a 2014 survey.[34] Other studies have shown confusion among nursing staff and housekeepers about who is responsible for cleaning particular equipment and services.[35-36] As Boyce et al demonstrated in one study, these factors can lead to considerable, measurable variance among different housekeepers with respect to "the amount of time spent cleaning surfaces, the number of wipes used in each room, and the level of cleanliness achieved."[37]

Surgical Risk

Patients undergoing surgery – particularly those receiving implants – have an increased risk of infection, not only from microbes on surfaces such as gowns and instruments, but from infectious airborne particles.

Unfortunately, preventative measures like air exchanges and positive air pressure rooms are undermined by room traffic and door openings, with a significant amount of contamination stemming from particulates originating from the hands, gowns or surgical instruments (including surgical smoke-emitting lasers or electrocautery tools) of OR personnel. In a research article published in Orthopaedics and Traumatology, D. Chauveaux noted that SSIs "due to intraoperative contamination are chiefly ascribable to airborne particles carrying microorganisms, mainly *Staphylococcus aureus*, which settle on the surgeon's hands and instruments. SSI prevention therefore rests on minimisation of airborne contaminated particle counts….". [38]

And the number of these airborne particles generated by normal OR activities can be significant. In their 2017 study, Noguchi et al measured a "large number of airborne particles"—a mean of 16,826 and 18,075 particles in the 0.3 to 0.5 micrometer size range—resulting from standard practices such as preparing instrument tables, gowning, and donning and doffing surgical gloves during total knee arthroplasty procedures.[39] The authors point out that these initially sterile particles can come in contact with unsterile areas such as skin (e.g. neck and face of surgical staff), walls, and floors, be

dispersed by airflow disruptions generated through door openings and foot traffic, and subsequently serve as vectors for bacterial transmission when they settle onto surgeons' hands, instruments, or the surgical wound itself.[39] In another study, Dalstrom et al demonstrated that the longer the procedure, the greater the risk for contamination by showing that the longer a surgical instrument tray is open and exposed in the OR, the greater the rate of contamination, with only 4 percent of trays contaminated at thirty minutes compared to 30 percent at four hours.[40]

Bacterial levels as high as 167 colony-forming units (CFUs) per cubic meter of air have been documented in operating rooms,[41] which represents a significant health risk to patients. One multicenter study showed that patients undergoing joint replacements in rooms with more than 50 CFUs of bacteria were 2.6 times as likely to have postoperative infections as those whose ORs contained 10 to 20 CFUs. The study's authors concluded that as airborne bacterial levels increase, infection rates increase in a linear fashion,[42] which comes with a hefty price tag both in terms of patient safety (i.e. periprosthetic joint infections [PJI] are associated with 2 to 7% mortality) and cost.[43-44] A 2017 study by Parvizi et al reported that the cost to a hospital of a single PJI was $100,000, with the overall cost to the U.S. healthcare system projected to reach nearly $1.6 billion by 2020.[43]

"No-Touch" Remedies: What Works?

Although there is a general consensus that patient rooms and other areas must be thoroughly and effectively cleaned on a regular basis, Boyce points out that over the years, there have been "areas of disagreement and controversy regarding best practices for cleaning and disinfection of environmental surfaces."[29]

While practice improvements such as checklists, a focus on high-touch surface areas, new antimicrobial chemicals, and environmental monitoring have helped reduce microbial load, surface and air contamination remains a real risk in healthcare facilities, contributing to the transmission of pathogens and endangering the health and lives of both patients and staff.

All of the approaches tried so far have helped to reduce the microbial load, but none has been overwhelmingly effective, and none has produced a sustained reduction in pathogens. In general, manual methods require a significant effort by cleaning personnel, only to have the bioburden begin to grow back as soon as the cleaning is complete.

This has led some experts to endorse "no-touch," automated room disinfection systems which, as stated by Otter et al., can mitigate the limitations of conventional disinfection methods that rely on the operator to ensure appropriate selection, formulation, distribution and contact time of the agent."[45]

The challenge, again as stated by Otter et al, is that many no-touch' systems, including ultraviolet radiation, hydrogen peroxide vapor systems, and aerosolized hydrogen peroxide (aHP), have important differences in their active agent, delivery mechanism, efficacy, process time and ease of use. Typically, there is a trade-off between time and effectiveness."[45]

Ultraviolet-C (UV-C) radiation devices often require less operation time than vapor technologies, but can be limited by other parameters. In a 2019 study, Mana et al reported that "the effectiveness of UV-C is reduced as distance from the device increases and in shaded areas, and residual pathogen contamination is not uncommon on surfaces after UV-C exposure." Other concerns include maintenance, the fiscal outlay for replacement bulbs, cycle time, and the degradative effect UV-C can have on surface materials, particularly plastics.[46-47] A large body of evidence demonstrates the extent to which UV-C radiation can cause discoloration, embrittlement, and aging of plastics, a ubiquitous component of healthcare materials.[47] This could theoretically pose an issue with warranties for these products if damage from UV-C is excluded from coverage.

In contrast to UV-C technology, Mana et al also reported that, while vapor technologies that emit hydrogen peroxide or peracetic acid are significantly more effective, they have an increased operating time – 1 to 3 hours versus 10 to 50 minutes for UV devices – thereby reducing room turnover. And while vapor (or "fogging") systems are used in many U.S. hospitals, "safety is a particular concern because both peracetic acid and hydrogen peroxide are strong oxidizing agents that have the potential to cause serious eye, skin, and respiratory tract irritation." Room vents and doors must be sealed beforehand, the room must be empty while the unit is in operation, and a hand-held sensor is needed to check for leaks and to ensure the room is safe to re-enter.[47] Moreover, researchers who conducted an assessment of the efficacy of vapor systems in a British ICU setting concluded that while hydrogen peroxide vapor was effective in eliminating bacteria from that environment, "the rapid rate of recontamination" after new patients were admitted "suggests that it is not an effective means of maintaining low levels of environmental contamination in an open-air intensive care unit."[48]

A Different Approach

The Synexis® DHP™ technology continuously uses dry hydrogen peroxide (DHP™) to reduce levels of harmful bacteria and viruses, fungi, and allergy-inducing molds in occupied spaces.

So how does it work? The system produces a gas, rather than a vapor, by catalytically combining converting ambient humidity and oxygen into dry hydrogen peroxide. Whether through a unit installed in an HVAC system at the diffuser level or a standalone unit, the DHP™ gas diffuses invisibly and continuously through the air, changing the concentration of gas particles in each cubic micron of air in the room to sanitize a targeted area.[5]

Microbes require water to survive and have electrostatically charged points on their cell surfaces that are designed to attract water molecules. Because DHP™ (H_20_2) molecules are very similar to water (H_20) molecules, they can attach to these charged points, attacking the microbes, disrupting their cell membranes, and incapacitating them.

In essence, the DHP™ cleans every part of the room that air touches – including hard and soft surfaces, floors, walls, windows, doors, and ceilings. And because a DHP™ unit runs continuously, there is less chance for cross-contamination and recontamination of surfaces.

A study by Herman et al., which used DHP™ technology for reduction of microbial colonization in a hospital setting, showed "a significant reduction in microbial colonization observed over seven days. Complete eradication of *S. aureus, Candida parapsilosis, Pseudomonas putida, Flavobacterium meningosepticum, Pseudomonas picketti,* and Citrobacter was seen at seven days. In addition, a reduction in *Alcaligenes* (68%), *Pseudomonas aeruginos*a (95%), and *Enterobacter* (50%) was seen from time of terminal cleaning to seven days."[13]

Herman's team concluded that this technology "has demonstrated potent dis-infective activity … against a variety of pathogenic microbes. The data strongly suggest that DHP™ effectively reduces microbial counts in the hospital setting, which may help reduce hospital-acquired infection rates."[13]

Similarly, in research published in the *American Journal of Infection Control,* researchers from a large pediatric oncology hospital found that use of DHP™ resulted not only in reductions of air bioburden, but also significant reductions of surface bioburden within treated intensive care unit rooms while also demonstrating a robust safety profile among what is arguably one of the most vulnerable populations.[14]

A new study using DHP™ adds to that body of evidence, showing a drastic reduction in bioburden on privacy curtains. These curtains represent a potential vector for cross-contamination as they are frequently touched by healthcare personnel and patient visitors.[49] DHP™ units significantly decrease that risk. Unlike UV-C light and hydrogen peroxide vapor produced by other "no-touch" automated systems, the DHP™ emitted by a Synexis unit is both effective in hard-to-reach areas and completely safe for room occupants,[14,50-51] producing concentrations of hydrogen peroxide of 0.005 to 0.025 parts per million (ppm)[51] – a fraction of the 1.0 ppm safety limit set by the Occupational Safety and Health Administration.[52] This DHP™ concentration is additionally far lower than the concentration of hydrogen peroxide in an aqueous droplet (over 1 billion molecules per cubic micron for just a 3% solution), lower than the continuous exposure safety limit (238 ppb Time Weighted Average), and **even lower than the equilibrium concentration of hydrogen peroxide maintained in our airways, lungs, and tears by the lactoperoxidase enzyme system** (10^{-6} Molar, or 602 molecules per cubic micron).[53-54]

DHP and COVID-19

The value of a microbial reduction solution that can safely and effectively operate in occupied settings to address microbes in the air and on surfaces has perhaps never been greater than it is now in the midst of the COVID-19 pandemic.

On October 5, 2020 the CDC updated their guidance on COVID-19 to acknowledge the likelihood for airborne spread of SARS-CoV-2, meaning that small virus-containing droplets or particles lingering in the air can infect people who are further than 6 feet away from the person who is infected or after that person has left the space. This position was supported by the investigation of COVID-19 cases spreading between people with no direct or indirect contact, suggesting that airborne transmission was the most likely route.[55] On December 8, 2020 the CDC went one step further in publishing updated ventilation recommendations designed to help improve air flow and to generate clean-to-

less-clean air flow within buildings—all with the goal of reducing the concentration of viral particles indoors.

In an effort to similarly reduce the concentration of SARS-CoV-2 viral particles on surfaces, the CDC has also issued guidance on environmental cleaning and disinfection across a spectrum of settings, ranging from healthcare facilities to schools. This guidance includes use of disinfectants that meet the EPA's criteria for use against SARS-CoV-2.

The EPA states that products approved to make claims against the enveloped virus SARS-CoV-2 must have demonstrated efficacy against harder-to-kill viruses.[56] Specifically, "If an antimicrobial product can kill a small, non-enveloped virus, it should be able to kill any large, non-enveloped virus or any enveloped virus. Similarly, a product that can kill a large, non-enveloped virus should be able to kill any enveloped virus."

DHP has not only demonstrated efficacy in reducing viral load of small, non-enveloped viruses in a number of studies, but also in reducing viral load of a gammacoronavirus, another member of the Coronavirus family. In fact, it reduced the level of the gammacoronavirus by over 99% within just 24 hours. These results show that DHP could be an effective weapon in the battle against the COVID-19 pandemic.

Conclusion

Given the enormous human and financial toll associated with HAIs – and in light of abundant evidence showing that reducing the level of bioburden mitigates the risk of infection – experts agree that adjunctive "no-touch" technologies can be a vital component of any effective environmental cleaning bundle designed to reduce risk for patients and healthcare workers alike.[4,61]

Unlike any of the other available "no-touch" technologies available today, the Synexis® dry hydrogen peroxide (DHP™) system offers a game-changing capability for the ongoing mitigation of microbial threats – even in occupied spaces and hard-to-reach areas. Operating invisibly around the clock, this innovative, patented technology produces a gas that drastically reduces microbial bioburden, even in remote and recessed areas of a room.

Since the discovery of hydrogen peroxide in the early 1800s, reams of research have demonstrated it to be a potent disinfectant. Other technologies focus on treating either just the air or just surfaces. Synexis® offers this well-established compound in a different vehicle – a natural, near ideal gas that, by continuously diffusing throughout all areas of a treated space, is capable of achieving microbial reduction both in air and on surfaces.

For more information, get in touch at Synexis.com/Contact.

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