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An overview of automated room disinfection systems: When to use them and how to choose them

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J.A. Otter[a], S. Yezli[b], F. Barbut[c,d], T.M. Perl[e]
[a]NIHR Health Protection Research Unit (HPRU) in HCAIs and AMR at Imperial College London, and Imperial College Healthcare NHS Trust, Infection Prevention and Control, London, United Kingdom, [b]Global Centre for Mass Gatherings Medicine, WHO Collaborating Centre for Mass Gatherings Medicine, Ministry of Health-Public Health Directorate, Riyadh, Kingdom of Saudi Arabia, [c]National Reference Laboratory for C. difficile, Infection Control Unit, Hôpital Saint Antoine, Paris, France, [d]INSERM S-1139, Faculté de Pharmacie de Paris, Université de Paris, Paris, France, [e]Infectious Diseases and Geographic Medicine, UT Southwestern Medical Center, Dallas, TX, United States

15.1 Introduction

As the role of contaminated surfaces in the transmission of nosocomial pathogens is increasingly recognized, there has been renewed emphasis on the importance of effective cleaning and disinfection (collectively described in this chapter as "environmental hygiene") [1,2]. This chapter considers the rationale for automated room disinfection (ARD) systems, which offer the potential to improve the efficacy and reliability of hospital disinfection. An assessment of the level of surface contamination that is a risk for transmission and understanding the limitations of conventional cleaning and disinfection methods is important to appreciate the potential of ARD systems. This chapter provides a detailed overview of the four classes of ARD system that are most commonly used in healthcare settings: aerosolized hydrogen peroxide (aHP), H_2O_2 vapor, ultraviolet C light (UVC), and pulsed-xenon UV (PX-UV). The differences between these systems in terms of their technological aspects, microbiological efficacy, evidence of clinical impact, and practicalities are described, along with a brief overview of other ARD systems and a consideration of their comparative effectiveness and cost. Based on these differences, the scenarios in which various ARD systems may be indicated are discussed in detail. Finally, future trends are considered.

15.2 Why consider an ARD system?

At one time, contaminated surfaces were thought to contribute negligibly to endemic transmission of pathogens in hospitals [3,4]. However, recent data indicate that contaminated surfaces make an important contribution to the endemic transmission of

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certain nosocomial pathogens [1,3,5]. The most convincing evidence comes from studies showing that admission to a room previously occupied by a patient colonized or infected with certain pathogens increases the risk of subsequent occupants acquiring these pathogens a factor of around two [1,6–11]. This association has been demonstrated for *Clostridium difficile*, vancomycin-resistant enterococci (VRE), methicillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii*, and *Pseudomonas aeruginosa* [1,7,9–11]. The epidemiological association is strengthened by the finding that improving terminal room disinfection reduces or eliminates this increased risk [8,12,13]. Thus, current terminal cleaning and disinfection following the discharge of patients with these pathogens is inadequate and needs to be improved. The increasing age and susceptibility of hospitalized patients, combined with the emergence of more virulent and epidemic strains of *C. difficile* such as 027/NAP1 and potentially untreatable multidrug-resistant Gram-negative bacteria such as pan-drug resistant *Acinetobacter baumannii*, carbapenemase-producing organisms, and certain viruses (for example the SARS Coronavirus), are further reasons to improve environmental decontamination [14,15].

The effectiveness of conventional cleaning and disinfection can be limited by several factors, including those associated with the products used and the procedure adopted. The key limitation is the reliance on a human operator to correctly select and formulate an appropriate agent and then to distribute it to all target surfaces for the necessary contact time. Improvement of these conventional methods requires modification of human behavior, which is difficult to achieve and sustain. The use of automated room disinfection systems (ARDs) provides an adjunctive approach, which removes or reduces reliance on the operator [16–19].

Automated systems have been adopted widely in other areas of healthcare to reduce reliance on operators and mitigate the potential for human error. Examples include robotic surgery and many aspects of critical care such as ventilators [20,21]. Indeed, commenting on the future of infection control in the late 1990s, Dr. Robert Weinstein wrote: "*Given the choice of improving technology or improving human behavior, technology is the better choice*." [22] In recognition of these potential benefits, publications about ARD systems have increased sharply in recent years.

Despite this recent interest, the concept of ARD is not new. Even before germ theory was formulated, "fumigation" was performed through burning sulfur and other chemical mixtures [23]. A paper published in 1901 provided a step-by-step guide on how to disinfect a "sick-room" through gaseous formaldehyde [24]. In the 1960s, formaldehyde was replaced by aerosolized chemicals such as quaternary ammonium compounds and phenolics due to concerns over toxicity and provided promising data on effectiveness [25–27]. However, concerns over efficacy and safety led to advice from the US Centers for Disease Control and Prevention (CDC) since the 1970s that disinfectant fogging should not be performed routinely in patient-care areas [27,28]. The increasing recognition of the importance of environmental contamination in transmission has prompted the development of several new ARD systems based on either hydrogen peroxide or ultraviolet (UV) radiation. The improved efficacy and safety of these systems compared with the disinfectant aerosolizers of the 1960s and 1970s have prompted a re-evaluation of the CDC recommendation [16].

This review considers the rationale for using ARD systems when conventional cleaning and disinfection requires improvement, compares the use of the key ARD systems in different scenarios, and discusses the role of regulators and professional societies in providing evidence-based adoption.

15.3 What level of surface contamination is a risk for transmission?

The relationship between the level of residual surface contamination after disinfection and the risk of transmission has not been studied in detail. The risk of transmission from an environmental surface depends on various factors, including the characteristics of the organism involved, patient susceptibility, and staff compliance with universal precautions and infection control policies (for example hand hygiene following contact with surfaces) [29–31]. The fact that subsequent occupants of a room vacated by a previously colonized or infected patient are at increased risk of infection indicates that conventional terminal cleaning and disinfection does not reduce contamination sufficiently to prevent transmission in these cases [1,6,7,9–11].

There is limited evidence that the risk of transmission is proportional to the level of surface contamination. Lawley et al. [32] developed a murine model and showed a dose-response relationship between the level of contamination in the cages and the proportion of healthy mice that developed *C. difficile* infection (CDI). All mice became infected when exposed for 1 hour to 100 spores/cm^2 and 50% became infected when exposed to 5 spores/cm^2. The concentration at which none of the mice became infected was less than one spore per cm^2. In the healthcare environment, room exposure times are usually measured in days and so the estimates by Lawley et al. are likely to be conservative. Lawley et al. then examined which disinfectants were able to interrupt the transmission of *C. difficile* and established a relationship between the level of inactivation of *C. difficile* spores in vitro and the degree to which transmission was interrupted (Fig. 15.1). Although data from animal studies should be interpreted with caution, these studies suggest that a low level of contamination can transmit spores to a susceptible host, and that there is a proportional relationship between the level of surface contamination and the degree of transmission.

The amount of shedding and the infective dose can be used to guide appropriate hospital cleaning and disinfection. Certain pathogens such as *C. difficile* and norovirus can be shed into the environment in high numbers and have a low infectious dose [1,33,34]. For example, the infectious dose for norovirus is 1–100 viral particles [34], while stool concentrations can reach $>10^{12}$ particles per gram[1] and up to 10^5 norovirus particles per 30 cm^2 have been identified on hospital surfaces [35]. Therefore, the presence of a pathogen on a surface at any concentration may be a risk for transmission. This is reflected in proposed guidelines for microbiological hygiene standards [36] and recent discussion surrounding the intended target for hospital disinfection [37,38].

However, in practice, a risk-based approach must be used when setting a target for an acceptable level of residual contamination, balancing patient safety with practicality

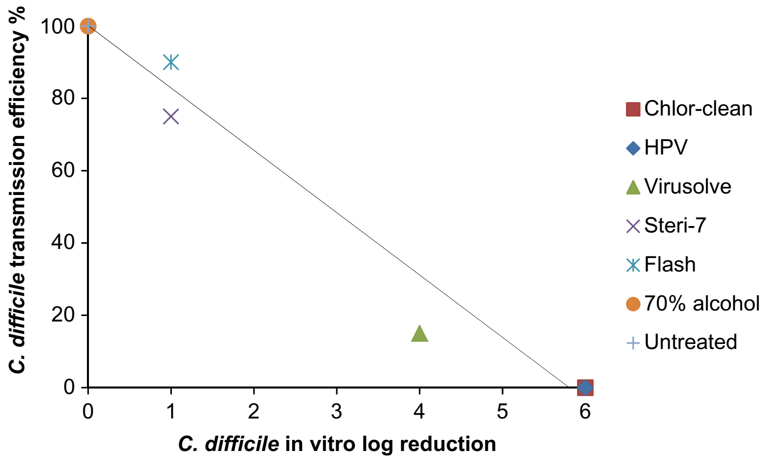

Fig. 15.1 Correlation between in vitro log reduction and interruption of transmission of *C. difficile* spores in a murine model. *HPV*, hydrogen peroxide vapor.
Data from Lawley TD, Clare S, Deakin LJ, et al. Use of purified Clostridium difficile spores to facilitate evaluation of health care disinfection regimens. Appl Environ Microbiol 2010;76:6895–900.

and cost, as is the case when selecting liquid disinfectants. More stringent targets should be set when the risk and/or consequences of infection are high, for example, for virulent, resistant, and/or highly infectious pathogens, especially in high-risk settings with immunocompromised patients [36–38]; a lower standard may be acceptable in lower risk settings.

15.4 Limitations of conventional cleaning and disinfection

Conventional cleaning and disinfection is performed by a human operator with liquid detergents or disinfectants. Microbiological studies indicate that conventional cleaning and disinfection without programs of targeted improvement rarely eradicate pathogens from surfaces [39–42]. For example, MRSA was identified on 66% of surfaces in patient rooms following terminal cleaning in one study [39] and *C. difficile* spores persisted despite bleach disinfection in another [43–45].

Problems associated with both "product" and "procedure" contribute to the failures of conventional cleaning and disinfection. These include the ineffectiveness of some agents against some pathogens (for example, many common hospital disinfectants are not effective against *C. difficile* spores [46,47] and norovirus [48]); toxicity to staff or the environment; damage to materials and equipment resulting in restrictions on usage [48,49]; certain agents are inhibited by organic matter on surfaces [47]; and there is a potential for biocide/antibiotic cross-resistance for some agents [50].

The key problem associated with the cleaning and disinfection procedure is the reliance on the operator to repeatedly ensure adequate selection, formulation, distribution, and contact time of the agent [46,51]. For example, a large assessment of conventional cleaning in 36 acute hospitals using fluorescent markers revealed that <50% of high risk objects in hospital rooms were cleaned at patient discharge [51]. Distribution of the active agent is difficult in the complex and intricate healthcare environment [51]. Ensuring the correct contact time to attain the microbial reduction achieved in vitro is particularly problematic because the disinfectant will evaporate from the surface [46]. The widespread presence of dry-surface biofilm also contributes to the failure of conventional methods because microbes in biofilms are more difficult to physically remove from surfaces and less susceptible to disinfectants [52–54]. Other problems include the delegation of responsibility for cleaning, which can fall between staff groups such as nurses and environmental hygiene staff particularly in the case of complex portable medical equipment [55]; difficulties in measuring the effectiveness of cleaning and disinfection [16] and achieving compliance with protocols/policies from an (often) poorly paid, poorly motivated workforce who may have limited spoken or written local language skills [56]; inadequate training and education of personnel [56]; inadequate time given to do the job properly [56]; insufficient (or nonexistent) cleaning prior to disinfection [47]; incorrect formulation of the disinfectant [50,57]; and contamination of cleaning solutions/materials [57,58].

Modifying human behavior is difficult but several different approaches can be taken, including routine microbiological analysis of surface hygiene, the use of fluorescent markers or ATP assays to assess the thoroughness of cleaning, feedback of cleaning performance, and education to enhance knowledge about the importance of the process [8,16,36,51,59,60]. The development of improved protocols and structured career progression for cleaning staff should be considered in addition to monitoring and feedback. This can improve the frequency of surfaces that are cleaned [51,61] and reduce the level of environmental contamination [62,63]. There is some evidence that improving the efficacy of conventional cleaning/disinfection can reduce the acquisition of pathogens [8,64–66]. For example, Hayden et al. [65] performed a 9-month prospective before-after study of educational improvements of cleaning and hand hygiene: the proportion of surfaces contaminated with VRE was reduced from 24% to 12% and patient acquisition of VRE was reduced from 33 to 17 acquisitions per 1000 patient-days. More recently, Mitchell et al. [66] performed a randomized controlled trial of an environmental hygiene bundle, which demonstrated improved cleaning performance and reduced HCAI for some organisms but not others [67]. Similarly, Datta et al. found that an educational improvement of cleaning performance reduced the rate of some organisms but not others [8]. These studies suggest that while improvements to conventional approaches to environmental hygiene can reduce transmission and HCAI, more can be done to maximize patient safety.

Few studies have evaluated the sustainability of such systematic improvements. One study showed that cleaning performance measured by the removal of a fluorescent marker increased from a baseline of 52% to 80%–85% through training and monthly feedback [68]. However, compliance soon returned toward baseline (57%–66%) when the monthly feedback ceased. Similarly, recent evidence indicates that altering the

location of fluorescent dye spots reduced the proportion of objects that were cleaned from 90% to approximately 60% [16].

In situations where the elimination of pathogens is required, even systematic improvement of conventional cleaning and disinfection may not be sufficient. Multiple rounds of disinfection with sodium hypochlorite (bleach), taking many hours [41,69], risking damage (corrosion) to materials [48,70] and presenting health risks for operators [49], can have limited success in removing environmental reservoirs of pathogens [35,40,41]. For example, an average of 2.8 rounds of quaternary ammonium compound disinfections were required to eradicate VRE from a room in one study [40] and *A. baumannii* or MRSA were cultured from 27% of rooms sampled after four rounds of cleaning and bleach disinfection [41]. ARD systems offer the potential to overcome some of these problems [17–19].

15.5 Overview of ARD systems

The most commonly used ARD systems in healthcare are aerosolized hydrogen peroxide (aHP) systems (such as Oxypharm Nocospray and Hygiene Solutions Deprox), H_2O_2 vapor systems (such as the Bioquell and Steris systems), UVC systems (such as Lumalier Tru-D), and pulsed-xenon-UV (PX-UV) systems (such as Xenex) [16–18,71–74].

Considering what would make an "ideal" ARD system is useful in comparing the features of the various systems available (Table 15.1). The "ideal" system would have a short cycle time; a high efficacy to eliminate pathogens from surfaces; and homogenous distribution of the active agent; the system should be easy to operate, fully automated, require minimal safety measures, allow instant access to the room, and have no environmental impact; finally, the system should have published evidence of clinical impact and the necessary regulatory approvals. Clearly, no single system meets all of these requirements and the importance of each feature will depend on the application.

15.5.1 Commonly used systems

15.5.1.1 Aerosolized hydrogen peroxide (aHP)

aHP systems deliver an aerosol of hydrogen peroxide. The systems used most commonly in healthcare use a solution containing 5%–6% hydrogen peroxide and <50 ppm silver (Fig. 15.2) [72,75–78]. These systems are sometimes known as "dry-mist hydrogen peroxide," though this term is a poor reflection of their properties [79,80]. Aerosolized droplets are introduced into an enclosure via a unidirectional nozzle [16,71]. One manufacturer (ASP Glosair) states a particle size of 8–10 μm [81,82] whereas another (Oxypharm Nocospray) states a smaller particle size of 0.5 μm [72]. The dose typically recommended for hospital rooms is 6 mL per m^3, although multiple cycles of this dose have been used in several studies [81,83]. Following exposure, the aerosol is usually left to decompose naturally, without any active aeration in most systems, although some have an active aeration system to reduce cycle times.

Table 15.1 An overview of "no-touch" automated room disinfection systems.

The "ideal" NTD system	Aerosolized hydrogen peroxide (aHP)	H_2O_2 vapor	UVC	Pulsed xenon UV (PX-UV)
Short cycle time (<1 h)	✘	✘	✓	✓
High level of microbial efficacy (6-log sporicidal reduction)	✘/✓	✓	✘	✘
Pathogens not culturable from surfaces after the cycle	✘	✓	✘	✘
Easy to operate	✓	✘	✓	✓
Fully automated operation	✓	✓	✘/✓	✘
Immediate room entry available[a]	✘	✘	✓	✓
No requirement of room sealing	✘	✘	✓	✓
Homogeneous distribution	✘	✓	✘	✘
Evidence of clinical impact	✘/✓	✓	✓	✘/✓

✓ = does meet the characteristic of the "ideal" NTD system.
✘ = does not meet the characteristic of the "ideal" NTD system.
✘/✓ = it is not clear whether or not the characteristic of the "ideal" NTD system is met.
[a] Immediate room entry may be advantageous in the event of an emergency.

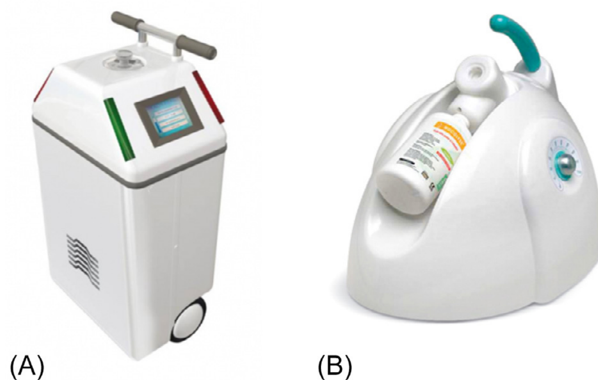

Fig. 15.2 Aerosolized hydrogen peroxide (aHP) systems. (A) Steris Biogienie. (B) Oxypharm Nocospray.

15.5.1.2 H_2O_2 vapor

H_2O_2 vapor systems deliver a heat-generated vapor of 30%–35% *w*/w aqueous hydrogen peroxide through a high-velocity air stream to achieve homogenous distribution throughout an enclosed area (enclosure) (Fig. 15.3) [71,76]. Two systems using H_2O_2 vapor are available commercially—Bioquell and Steris. Bioquell systems are usually termed hydrogen peroxide vapor (HPV) and Steris systems vaporized hydrogen

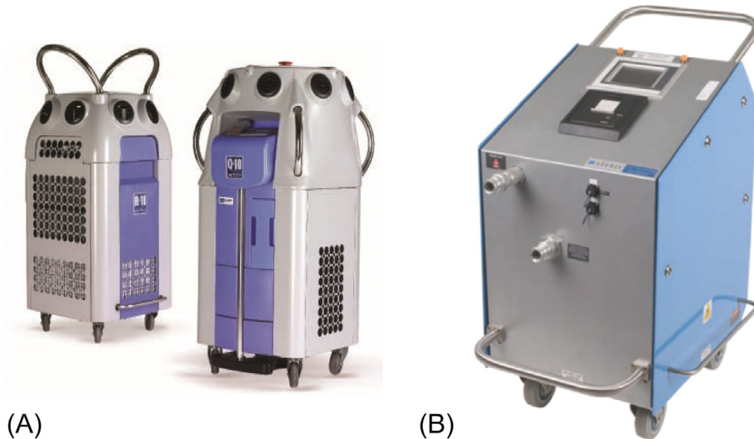

Fig. 15.3 H_2O_2 vapor systems. (A) Bioquell hydrogen peroxide vapor (HPV). (B) Steris vaporized hydrogen peroxide (VHP).

peroxide (VHP). Bioquell HPV includes a generator to produce HPV including a module to measure the concentration of HPV, temperature, and relative humidity in the enclosure and an aeration unit to catalyze the breakdown of HPV to oxygen and water vapor after HPV exposure. A control pedestal is situated outside the enclosure to provide remote control. Bioquell HPV is delivered until the air in the enclosure becomes saturated and hydrogen peroxide begins to condense on surfaces [84,85]. Steris VHP systems have a generator inside the room with an integral aeration unit and dehumidifier designed to achieve a set humidity level prior to the start of the cycle. The system is controlled remotely from outside the enclosure. Steris VHP systems deliver "noncondensing" VHP by drying the vapor stream as it is returned to the generator. Bioquell systems do not control the H_2O_2 air concentration while the Steris systems hold a steady H_2O_2 air concentration throughout the exposure period.

15.5.1.3 Ultraviolet C radiation (UVC)

UVC systems for room decontamination deliver-specific doses (for example, 12,000 μWs/cm^2 for vegetative bacteria and 22,000–36,000 μWs/cm^2 for spores) of UVC (254 nm range) to surfaces (Fig. 15.4) [86–88]. Most manufacturers recommend multiple cycles from different locations to reduce issues due to line of sight [86]. Some UVC systems contain sensors to measure the amount of UVC light reflected back to the device to confirm the delivery of a specified dose to all parts of the room.

15.5.1.4 Pulsed-xenon UV (PX-UV)

PX-UV systems emit broad spectrum UV in short pulses (Fig. 15.4) [89]. They are placed at multiple room locations and have a relatively short cycle time.

Fig. 15.4 Ultraviolet radiation systems. (A) UVC: Lumalier Tru-D. (B) Pulsed xenon UV (PX-UV): Xenex.

15.5.2 Microbiological efficacy

Studies evaluating the in vitro and in situ efficacy of ARD systems are summarized in Tables 15.2 and 15.3, respectively. aHP systems achieve a ~4-log reduction on *C. difficile* spores in vitro [80] and have limited capacity to inactivate commercially produced 6-log spore biological indicators (BIs) [81,83]. Catalase-positive bacteria are considerably less susceptible to the low concentration of hydrogen peroxide used by aHP systems than catalase-negative bacteria or metabolically inert spores [90,91]. The efficacy of aHP systems against catalase-positive bacteria remains to be firmly established, with conflicting published data on the level of inactivation of MRSA and *A. baumannii* [82,92] and tuberculocidal activity [79,93–95]. aHP systems have been shown to reduce contamination of *C. difficile* and MRSA on hospital surfaces but have not been shown to eradicate pathogens in clinical practice [72,77,78,80,96]. For example, one or more positive *C. difficile* cultures were collected from 20% of 15[80] and 50% of 10[77] rooms studied after an aHP process.

Both Bioquell HPV and Steris VHP systems are EPA-registered sterilants, which means they have passed the AOAC sporicide test on porous and nonporous surfaces [47]. Both systems are associated with the eradication of pathogens from surfaces *in situ* [41,43,69,85,97–100] and cycles are validated by a >6-log reduction of *Geobacillus stearothermophilus* biological indicator (BI) spores [43,69,97,98]. HPV and VHP are sporicidal, bactericidal, mycobactericidal, and virucidal, achieving a >6-log reduction

Table 15.2 Studies evaluating the in vitro efficacy of "no-touch" automated room disinfection systems.

Author	Year	Setting	Design	Results
H_2O_2 vapor				
Petit et al. [106]	2017	30 m^3 airlock chamber	Foot and mouth disease virus was inoculated onto stainless steel discs and exposed to HPV.	A >6-log reduction was achieved throughout the chamber.
Murdoch et al. [108]	2016	Laboratory enclosure	The efficacy of 5, 10, and 35% H_2O_2 was evaluated against MRSA and *Geobacillus stearothermophilus* dried onto stainless steel discs.	A "dose-response" type relationship was established between the concentration of H_2O_2 vapor and biocidal efficacy.
Ali et al. [182]	2016	Hospital room	Stainless steel coupons were inoculated with MRSA, *K. pneumoniae*, and *C. difficile*.	A >5-log reduction was achieved on all coupons.
Lemmen et al. [183]	2015	Operating room	Stainless steel and cotton carriers containing MRSA, VRE, or MDR A baumannii were placed at 4 locations in the OR and exposed to HPV.	A >4-log reduction was achieved on all organisms at all four locations in the room.
Barbut et al. [104]	2012	33–45 m^3 rooms, unfurnished, unoccupied.	Plastic or laminate carriers with 5–6 log of *C. difficile* spores exposed to HPV.	*C. difficile* was completely eradicated from the exposed carriers regardless of the *C. difficile* strain or surface used
Otter et al. [107]	2012	A 100 m^3 test room	MRSA carriers containing 6.1–7.3 log of MRSA suspended in distilled water, 0.3%, 3%, or 10% BSA, TSB, or 0.9% saline and dried on stainless steel discs were exposed to HPV.	The effectiveness of HPV was reduced in a step-wise manner as type and concentration of simulated soiling increased. No MRSA was recovered from any of the carriers after 60 min exposure to HPV.
Havill et al. [152]	2012	15 patient rooms with bathrooms (46–86 m^3)	Carrier disks with ~10^6 *C. difficile* spores and BIs with 10^4 and 10^6 *G. stearothermophilus* spores were placed in 5 sites (3 sites were not in direct line of sight from the HPV generator).	HPV achieved >6-log reduction on *C. difficile* in all 5 sites. HPV inactivated 99% (74/75) of 6-log BIs and 100% (75/75) of 4-log BIs.

Fu et al. [82]	2012	Two rooms to simulate a patient room (50.1 m^3) and an en-suite bathroom (13.2 m^3)	Pouched and unpouched 4- and 6-log *G. stearothermophilus* BIs and in-house prepared test discs containing ~10^6 MRSA, *C. difficile* spores and *A. baumannii* were placed at 11 locations in the test area.	HPV inactivated 91% (40/44) of the pouched 6-log BIs and 95% (42/44) of the pouched 4-log BIs. The HPV system completely inactivated (>6-log reduction) MRSA dried in water from all replicates in 9/11 locations, *A. baumannii* dried in water from all replicates in 6/11 locations, and *C. difficile* from all replicates in all locations.
Bentley et al. [105]	2012	A class II safety cabinet	FCV virus was dried on 1 cm^2 carriers of stainless steel, glass, vinyl flooring, ceramic tile, or PVC.	>4-log reduction was achieved on all surfaces after HPV.
Holmdahl et al. [81]	2011	A purpose-built 136 m^3 test room	6-log Tyvek-pouched *G. stearothermophilus* BIs were placed at 20 locations in the first test and 14 locations in another 2 tests.	HPV inactivated 100% (48/48) of 6-log BIs.
Berrie et al. [101]	2011	A microbiology safety cabinet	Recombinant adenovirus (Ad5GFP) was dried on 10 mm-diameter stainless steel discs at concentrations of 7.6–9.4 log $TCID_{50}$/disc.	HPV achieved a >8-log $TCID_{50}$ reduction in virus titer.
Pottage et al. [90]	2011	A test chamber (20.7 m^3)	Stainless steel indicators of ~10^6 MRSA or ~10^6 commercially available *G. stearothermophilus* BIs were exposed to Steris VHP in a test chamber. BIs were removed and enumerated at timed intervals.	After 30 min exposure to VHP there was ~3-log reduction in MRSA and ~5-log reduction *G. stearothermophilus* spores, indicating that the catalase-positive MRSA are less susceptible to VHP than the metabolically inert spores.
Pottage et al. [103]	2010	A class III safety cabinet	MS2 bacteriophage was dried on 10 mm-diameter stainless steel discs at concentrations of 7–9-log pfu/carrier. MS2 phage was also dried in 10% or 50% horse blood. Inoculated carriers were exposed to either VHP (Steris) or HPV (Bioquell).	HPV caused >6-log reduction on the phage; VHP caused a 5–6 log reduction on the phage. Reductions for HPV were 5.8 and 2.7 when the virus was dried in 10% and 50% horse blood, respectively. Reductions for VHP were >9 and 3.5 when the virus was dried in 10% and 50% horse blood, respectively.

Continued

Table 15.2 Continued

Author	Year	Setting	Design	Results
Otter et al. [91]	2009	A 100 m^3 test room	5 strains of MRSA and 3 stains of VRE, *Acinetobacter* sp., *K. pneumoniae*, and *C. difficile* spores were dried on stainless steel discs at concentrations of 5–7-log cfu/carrier in either water or BSA to simulate soiling.	All carriers were inactivated after exposure to HPV when dried from water or 0.3% BSA.
Hall et al. [84]	2007	A biological safety cabinet and a BSL III laboratory room (37 m^3)	~3-log *M. tuberculosis* dried on stainless steel carriers were exposed to HPV in a biological safety cabinet and at 10 locations in a BSL III laboratory room. 6-log *G. stearothermophilus* BIs were also exposed to HPV in the room experiment.	No *M. tuberculosis* BIs grew after 30 min exposure to HPV in the safety cabinet. In the room experiment, all *M. tuberculosis* and *G. stearothermophilus* BIs were inactivated at all 10 locations following exposure to HPV for 90 min.
Johnston et al. [184]	2005	A 0.4 m^3 glovebox enclosure	> 6-log of 2 strains of *C. botulinum* spores dried on stainless steel discs and 6-log *G. stearothermophilus* BIs were exposed to HPV.	After 7 min exposure to HPV, all *C. botulinum* spores were inactivated. No viable *G. stearothermophilus* spores were recovered after 6 min exposure to HPV.
Kahnert et al. [185]	2005	A 64.5 m^3 laboratory room	8×10^4–2.3×10^6 of 2 strains of *M. tuberculosis* were dried on tissue culture plates, placed in steam-permeable Tyvek pouches, distributed at 4 locations in the test room, and exposed to Steris VHP.	No viable *M. tuberculosis* was recovered at any of the locations after exposure to VHP.
Aerosolized hydrogen peroxide (aHP)				
Montazeri et al. [186]	2017	A BSL-3 laboratory	Human norovirus and feline calicivirus (FCV) were dried onto steel coupons and exposed to 7.5% hydrogen peroxide aerosol at 12 mL/m^3.	A <3 log reduction was achieved on human norovirus, and a >4-log reduction on FCV.
Zonta et al. [187]	2016	Laboratory 4 m^3 test chamber	Steel discs and glass slides were inoculated with murine norovirus and feline calicivirus and exposed to 7% nebulized hydrogen peroxide.	A ≥4 log reduction was achieved on all samples tested.

Ali et al. [182]	2016	Hospital room	Stainless steel coupons were inoculated with MRSA, *K. pneumoniae* and *C. difficile.*	A >5-log reduction was achieved on all coupons.
Steindl et al. [188]	2015	Test room	Spore suspensions of 2 *C. difficile* strains were dried onto ceramic tiles and exposed to 7.5% hydrogen peroxide aerosol.	After 2 h of exposure, no spores were recovered, representing a >5-log reduction on both strains.
Fu et al. [82]	2012	Two rooms to simulate a patient room (50.1 m^3) and an en-suite bathroom (13.2 m^3)	Pouched and unpouched 4- and 6-log *G. stearothermophilus* BIs and in-house prepared test discs containing ~10^6 MRSA, *C. difficile* spores and *A. baumannii* were placed at 11 locations in the test area.	aHP inactivated 13.6% (6/44) of the unpouched 6-log BIs, and 36.4% of the unpouched 4-log BIs. aHP generally achieved a <4-log reduction on MRSA, *A. baumannii*, and *C. difficile* spores. The level of inactivation varied considerably by room location.
Holmdahl et al. [81]	2011	A purpose-built 136 m^3 test room	6-log Tyvek-pouched *G. stearothermophilus* BIs were placed at 20 locations in the first test and 14 locations in another 2 tests. Three back-to-back aHP cycles using 2 aHP machines was run.	aHP inactivated 50% (24/48) of BIs; 10% (2/20) of BIs in the first test and 79% (22/28) of BIs in the other 2 tests were inactivated.
Piskin et al. [92]	2011	A single hospital isolation room (53 m^3)	Stainless steel discs carriers inoculated with ~4.5-log MRSA or *A. baumannii* dried from water or 5% sterile serum were placed at various locations in the test room.	Log reductions of ~4 were achieved on MRSA and *A. baumannii*. aHP was less effective for the bacteria dried in serum and in closed or semiclosed locations (e.g. inside a drawer).
Koburger et al. [189]	2011	37 m^3 test room	Carriers inoculated with 4.28, 5.48, and 6.5-log of *Aspergillus brasiliensis.*	aHP achieved 0.38, 1.27, and 4.28-log reductions respectively at the initial fungal loads of 6.5, 5.48, and 4.28-log.
Andersen et al. [79]	2010	TB laboratory (BSL3)	Plastic plates inoculated with ~3×10^4 *M. tuberculosis* and placed in an open box (lid off) on an open bench. This room was treated with 3 or 6 aHP cycles.	*M. tuberculosis* growth was observed in all TB broth media (20/20) after 10–21 day incubation.

Continued

Table 15.2 Continued

Author	Year	Setting	Design	Results
Grare et al. [95]	2008	80 m^3 BSL3 laboratory	Cotton tissues inoculated with 10^5–10^6 dried *M. tuberculosis* were placed in various room locations.	aHP achieved >5-log reduction on *M. tuberculosis* in all room locations.
Bartels et al. [96]	2008	Hospital room	5 different locations (20–100 cm^2) in the room were inoculated with 100 cfu/cm^2 (3–4-log) of MRSA cultures diluted in urine. One or 3 aHP decontamination cycles were run.	All samples were negative after 1 or 3 aHP cycles.
Andersen et al. [83]	2006	Hospital rooms (4–58 m^3) and garages (120–200 m^3)	6-log *B. atrophaeus* spore BIs were used. BIs were placed at various locations in rooms, ambulances parked in garages, and on the outside and inside of medical equipment.	One or two aHP cycles had no effect on BIs. 3 aHP cycles inactivated 87% (127/146) of BIs in two test rooms, 62% (137/220) of BIs on or in medical equipment and all BIs (60/60) in the ambulances.
Ultraviolet C radiation (UVC)				
Cadnum et al. [83a]	2019	Radiology procedure room	8 UV devices tested in parallel for their ability to inactive MRSA, VRE and *C. difficile* dried onto stainless steel carriers.	
Smolle et al. [190]	2018	Hospital room	Textiles inoculated with *Enterococcus faecium* were disinfected using UVC.	UVC achieved a significant 1.4 log reduction on *E. faecium.*
Ali et al. [190a]	2017	Hospital rooms	6 hospital rooms were disinfected using 2 UV systems; stainless steel coupons inoculated with MRSA, CPE, and *C. difficile* were placed at 5 room locations.	Both systems demonstrated 4–5 log reductions in MRSA and CPE at low soiling; reductions in *C. difficile* spores ranged from 0.1 to 5 log depending on the system, room location, and soil level.
Bedell et al. [191]	2016	Biosafety cabinet	Mouse hepatitis virus (MNV) and MERS-CoV were dried onto glass coverslips and exposed to UVC.	A >5-log reduction was achieved on MHV within 10 min of exposure, and on MERS-CoV within 5 min of exposure.

Havill et al. [152]	2012	15 patients rooms (with bathrooms) (46–86 m^3)	Carrier disks with ~10^6 *C. difficile* spores and BIs with 10^4 and 10^6 *G. stearothermophilus* spores were placed in 5 sites (3 sites were not in direct line of sight from the UVC unit) and exposed to 22,000 μWs/cm^2.	UVC achieved a mean of 2.2 log reduction on *C. difficile* (range 1.7–3 log reduction). UVC inactivated 29% (22/75) of 4-log BIs (range 7%–53%) and 0% (0/75) of 6-log BIs. UVC was significantly less effective out of direct line of sight.
Boyce et al. [86]	2011	25 patients rooms (with bathrooms) (46–86 m^3)	Carrier disks with ~10^5 *C. difficile* spores were placed in 5 sites (3 sites were not in direct line of sight from the devices) using a 1- (22,000 μWs/cm^2) or 2-stage procedure.	1-stage procedure: 68-min median cycle time and mean of 2.2 log reduction (range 1.7–2.9 log reduction). 2-stage procedure: 84 min median cycle time and mean of 2.3 log reduction (range 1.4–3.2 log reduction). UVC was significantly less effective out of direct line of sight.
Nerandzic et al. [87]	2010	Laboratory bench top	*C. difficile* spores, MRSA and VRE suspended in PBS or 10 mg/ml BSA were dried on bench tops (1 cm^2) at 3–5 log. Inactivation of pathogens was assessed at reflected doses ranging from 5000 to 22,000 μWs/cm^2.	Sporicidal cycle (22,000 μWs/cm^2) achieved reductions of >2–4 for MRSA, *C. difficile* and VRE. Increasing the dose from 5000 to 20,000 μWs/cm^2 increased efficacy for *C. difficile* spores (from 1.1 to 2.7 log) but not for VRE or MRSA. Suspending medium or room location did not affect log reductions significantly.
		Hospital rooms	Plastic carriers with ~10^5 *C. difficile* spores were placed around the room and exposed to 22,000 μWs/cm^2 (sporicidal cycle).	UVC achieved a 2.6-log reduction on carriers in direct line of sight and 1-log reduction on carriers out of direct line of site.
			Staphylococcus warneri was dried on 1 cm^2 areas on 26 frequently touched sites and on 20 portable equipment sites at 4–5 log and exposed to 12,000 μWs/cm^2 (vegetative cycle).	UVC achieved a ~3.5-log reduction on the 26 environmental sites and a 2-log reduction on equipment.

Continued

Table 15.2 Continued

Author	Year	Setting	Design	Results
Rutala et al. [88]	2010	Patient rooms with bathroom	MRSA, VRE, *A. baumannii*, or *C. difficile* spores were dried on formica sheets (64 cm^2) at ~10^4–10^5 cfu, placed at various room locations and exposed to 36,000 $\mu Ws/cm^2$ for *C. difficile* (sporicidal cycle) or 12,000 $\mu Ws/cm^2$ (vegetative cycle) for the other organisms.	UVC achieved mean log reduction of 2.79 for *C. difficile*, 3.88 for *A. baumannii*, 3.46 for VRE, and 3.94 for MRSA. UVC was less effective for sites that are out of line of sight.
Pulsed-xenon UV (PX-UV)				
Cadnum et al. [83a]	2019	Radiology procedure room	8 UV devices tested in parallel for their ability to inactive MRSA, VRE, and *C. difficile* dried onto stainless steel carriers.	The PX-UV device achieve a <1-log reduction on MRSA, VRE, and *C. difficile*; PX-UV was less effective than UVC systems.
Nerandzic et al. [112]	2015	Hospital room	Glass discs seeded with *C. difficile*, MRSA, and VRE were exposed to PX-UV.	PX-UV achieved a <1-log reduction on VRE and *C. difficile*, and a <2-log reduction on MRSA.

Table 15.3 Studies evaluating the in situ efficacy of "no-touch" automated room disinfection systems.

Author	Year	Setting	Design	Samples contaminated
HPV				
French et al. [39]	2004	A 1200-bed London teaching hospital	Environmental sampling for MRSA was conducted in MRSA-patient side rooms and bathrooms before and after HPV decontamination.	Before decontamination, 61 (72%) of 85 sites were positive for MRSA; 72% by direct plating. After HPV, one (1.2%) of the 85 sites (a floor corner in one of the rooms) yielded MRSA, by selective broth enrichment. Rooms were not cleaned prior to HPV decontamination.
Jeanes et al. [69]	2005	A UK hospital surgery ward	Environmental sampling for MRSA was conducted before and after HPV decontamination.	Before decontamination, 8 (16.0%) of 50 swabs taken were positive for MRSA. After HPV, none (0%) of the 50 swabs yielded MRSA.
Bates et al. [97]	2005	A UK hospital NICU	Environmental sampling of the NICU was conducted before and after HPV decontamination	Before decontamination, 2 (4.8%) and 4 (9.5%) of the 42 sites samples were positive for *Serratia* and MSSA respectively. After HPV, none (0%) of the 25 sites samples yielded *Serratia* or MSSA.
Boyce et al. [192]	2006	A 500-bed university hospital	Surfaces in 4 wards and 3 patient rooms were sampled using moistened swabs before and after HPV decontamination.	Before decontamination, 8 (4.8%), 9 (5.5%), and 23 (13.9%) of the 165 sites samples were positive for *C. difficile*, MRSA, and VRE, respectively. After HPV, none (0%) of the 155 sites samples yielded *C. difficile*, MRSA, or VRE.
Hardy et al. [98]	2007	A 9-beded open plan ICU	Environmental sampling for MRSA in the ICU was conducted using cotton swabs before and after HPV decontamination.	Before decontamination, 5 (17.2%) of 29 sites sampled were positive for MRSA. After HPV, none (0%) of the 25 sites sampled yielded MRSA.

Continued

Table 15.3 Continued

Author	Year	Setting	Design	Samples contaminated
Otter et al. [157]	2007	A 500-bed hospital	Standardized sites in a single-occupancy ward side-room with an en-suite bathroom were sampled for MRSA, GNR and VRE using cotton swabs before and after HPV decontamination.	MRSA was isolated from 12 (40.0%) and 1 (3.3%) of the 30 sites sampled before and after HPV respectively. GNR was isolated from 3 (10.0%) and none (0%) of the 30 sites sampled before and after HPV, respectively. VRE was isolated from 1 (6.7%) and none (0%) of the 15 sites sampled before and after HPV, respectively.
Boyce et al. [43]	2008	A 500-bed university hospital	Surfaces in patient rooms, bathrooms, and open ward areas were sampled for *C. difficile* using sponges before and after HPV decontamination.	Before decontamination, 11 (25.6%) of the 43 sites samples were positive for *C. difficile*. After HPV, none (0%) of the 37 sites samples yielded *C. difficile*.
Dryden et al. [114]	2008	A 28-bed surgical ward	Moistened swabs were used to sample multiple surfaces for MRSA before and after HPV decontamination.	Before decontamination 8 (27.6%) of 29 sites sampled were positive for MRSA. After HPV, one (3.4%) of the 29 sites (a composite swab from six bed-rails) yielded MRSA.
Otter et al. [100]	2008	A 39-bed neonatal unit (NNU)	Environmental sampling for the outbreak strain of *S. aureus* was conducted in the NNU before and after HPV.	Before decontamination 3 (4.0%) of 74 sites sampled were positive for *S. aureus*. After HPV, none (0%) of the 64 sites sampled yielded *S. aureus*.
Otter et al. [99]	2010	A 12-bed ICU	Environmental sampling was conducted in the ICU using moistened cotton swabs before and after HPV.	Before decontamination 10 (47.6%) of 21 sites sampled were positive for GNRs including MDR *E. cloacae*. After HPV, none (0%) of the 63 sites sampled yielded GNRs.
[a]Ray et al. [85]	2010	A 54-bed long-term acute care hospital	Environmental sampling for *A. baumannii* was conducted in the wards using moistened cotton swabs before and after VHP.	Before decontamination 8 (8.6%) of 93 sites sampled were positive for *A. baumannii* including MDR *A. baumannii*. None of the sites sampled after VHP yielded *A. baumannii*.

Manian et al. [41]	2011	A 900-bed tertiary care hospital	Moistened culture swabs were used to sample rooms for MRSA and *A. baumannii* complex (ABC) before and after HPV.	Before decontamination, 6 (0.8%) of 740 sites were positive for MRSA and 6 (0.8%) of 740 sites were positive for ABC. After HPV, none (0%) of the 740 sites samples were positive for MRSA or ABC.
Barbut et al. [193]	2012	A burns unit	Environmental sampling of surfaces in individual patient's rooms before and after HPV.	Before decontamination, 6% (6/102) of surface samples were positive for *Acinetobacter*, 4% (4/102) were positive for *S. aureus* and 2% (2/102) were positive for *E. coli*. No pathogens were isolated from surfaces after HPV.
			Environmental sampling of surfaces in individual patient's rooms before and after HPV.	Before decontamination, 4% (3/66) and 7% (1/14) of the fungal surface and air samples, respectively, were positive for *Aspergillus* spp., while 1% (1/92) of the bacterial surface samples yielded *S. aureus*. No pathogens were isolated from surfaces or the air after HPV.
Ali et al. [182]	2016	Hospital room	Contact plates were used to sample 22 sites in 10 hospitals rooms after conventional disinfection and again at HPV.	A significant reduction in surface contamination was demonstrated.
Aerosolized hydrogen peroxide (aHP)				
Shapey et al. [77]	2008	A UK hospital	Environmental sampling for *C. difficile* of clinical areas was performed using moistened cotton swabs before and after aHP.	*C. difficile* was isolated from 48 (23.6%) of 203 swabs taken before aHP and from 7 (3.4%) of 203 of the swabs taken after aHP.
Bartels et al. [96]	2008	A Danish hospital	14 upholstered chairs involved in an MRSA outbreak were sampled before and after decontamination with aHP.	Before decontamination, 4 (28.6%) of 14 chairs were positive for MRSA. After aHP, 1 (7.1%) of 14 chairs yielded MRSA.

Continued

Table 15.3 Continued

Author	Year	Setting	Design	Samples contaminated
Barbut et al. [104]	2009	A French hospital	Environmental surfaces from rooms of patients with CDI were sampled for *C. difficile* using moistened swabs before and after aHP disinfection.	Before decontamination 34 (18.9%) of 180 sites sampled were positive for *C. difficile*. After aHP, 4 (2.2%) of 180 sites yielded *C. difficile*.
Ali et al. [182]	2016	Hospital room	Contact plates were used to sample 22 sites in 10 hospital rooms after conventional disinfection and again at aHP.	A significant reduction in surface contamination was demonstrated.
Yui et al. [194]	2017	A UK hospital	Surfaces were sampled after exposure to aHP terminal disinfection for patients with CDI.	*C. difficile* was culture from 131 of 572 surfaces (22.9%) before terminal cleaning, on 105 of 959 surfaces (10.6%) after terminal cleaning, and on 43 of 967 surfaces (4.4%) after hydrogen peroxide disinfection.
Ultraviolet C light (UVC)				
Nerandzic et al. [87]	2010	A 202-bed acute care hospital	Motioned swabs were used to sample 4 sites for MRSA, VRE, and *C. difficile* from rooms of 66 discharged patients before and after a sporicidal UVC treatment (22,000 μWs/cm^2).	Before decontamination, MRSA, *C. difficile*, and VRE were isolated from 28 (10.7%), 9 (3.4%), and 7 (2.7%) of the 261 sites sampled, respectively. After UVC, MRSA, *C. difficile*, and VRE were respectively isolated from 2 (0.8%), 1 (0.4%), and 1 (0.4%) of the 261 sites sampled, respectively. Rooms were not cleaned prior to UVC treatment.
Rutala et al. [88]	2010	An acute care tertiary hospital	Sites in rooms that had housed patients with MRSA or VRE were sampled using Rodac plates before and after a vegetative UVC cycle (12,000 μWs/cm^2).	Before decontamination, 81 (20.3%) of the 400 sites sampled were positive for MRSA. After UVC, 2 (0.5%) of the 400 sites sampled yielded MRSA. Rooms were not cleaned prior to UVC treatment.

Ali et al. [190a]	2017	Hospital rooms	6 hospital rooms were sampled after 2 different UVC systems were used.	UV disinfection eliminated contamination after terminal cleaning in 8/14 (57%) and 11/14 (79%) sites.
Mustapha et al. [195]	2018	Hospital floors	Comparison of conventional QAC disinfection alone with QAC disinfection + UVC.	Floor disinfection resulted in a significant reduction in contamination with pathogens; MRSA was identified on 9% of floors tested after conventional disinfection and 1% after UVC disinfection.
Pulsed-xenon UV (PX-UV)				
Stibich et al. [89]	2011	A cancer center	Surfaces were sampled in rooms that had housed VRE patients using moistened swabs before and after PX-UV exposure.	Before decontamination, 4 (4.4%) of the 91 sites sampled were positive for VRE. After UV treatment, none of the 75 sites sampled yielded VRE.
Beal et al. [109]	2016	UK hematology unit	PX-UV was used following terminal disinfection; contact plates and surface swabbing was used to evaluate microbiological impact.	There was a 76% reduction in the total colony count (TCCs) following manual cleaning, with an additional 14% reduction following PX-UV, resulting in an overall reduction of 90% in TCCs. The proportion of 80 sites contaminated with VRE was 32.5% after manual cleaning and 20% after PX-UV.

[a] This study relates to the Steris VHP system; all other HPV studies relate to the Bioquell HPV system.

against a wide range of nosocomial pathogens including *C. difficile* spores, MRSA, VRE, *A. baumannii*, and norovirus surrogates [84,91,101–106], though efficacy may be reduced by high microbial loading and the presence of organic soil [82,91,103,107]. An in vitro study established a dose-response relationship between the concentration of hydrogen peroxide used in an HPV system and the microbiological efficacy [108]. This is helpful in understanding why aHP systems, which use a lower concentration of hydrogen peroxide, are less effective than HPV/VHP systems, which use a higher concentration of hydrogen peroxide.

UVC produces a dose-dependent 2 to 4-log reduction of nosocomial pathogens experimentally dried onto surfaces [86–88] but the microbiological reduction is significantly lower out of direct line of sight of the device [86–88]. For example, in one study, a 1-log reduction was achieved on *C. difficile* spores inoculated on plastic carriers placed 10 ft away from the device out of direct line of sight, compared with 2.6-log in direct line of sight [87]. Several studies of one UVC system (Lumalier Tru-D) indicated a significant reduction of surface contamination measured by total aerobic count or sampling for specific pathogens [86–88]; however, there was incomplete inactivation of *C. difficile*, VRE, *Acinetobacter*, or MRSA on hospital surfaces [86–88].

A PX-UV system (Xenex) achieved a significant reduction in VRE contamination in a room in a 12-min cycle [89]. Several studies have shown that PX-UV reduce the concentration of bacteria on hospital surfaces [109–111]. However, a head-to-head evaluation of a UVC and pulsed-xenon UV system showed that the UVC system achieved a high level of efficacy in vitro when operated for the same amount of time from the same point in the room [112]. This study showed that that UVC system achieved a >3-log reduction on VRE whereas the PX-UV system achieved a <1-log reduction.

15.5.3 Clinical impact

There is emerging evidence that ARD systems improve patient outcomes (see Table 15.4).

15.5.3.1 H_2O_2 vapor

HPV has been used to remove environmental reservoirs during outbreaks of *C. difficile* [113], MRSA and methicillin-susceptible *S. aureus* (MSSA) [69,100,114], multidrug-resistant Gram-negative bacteria [97,99,115] and other pathogens [116]. VHP has been used for tackling environmental reservoirs during outbreaks of *A. baumannii* in two reports [85,117]. The clinical impact of VHP aside from outbreak settings is not reported. On the other hand, three studies have assessed the impact of HPV in the setting of endemic infections. A prospective cohort study by Passaretti et al. demonstrated that patients admitted to rooms vacated by patients with multidrug-resistant organisms (MDROs) and disinfected using HPV were 64% less likely to acquire MDROs than patients admitted to such rooms disinfected using standard methods [13]. Thus, HPV decontamination successfully mitigated the risk from the prior room occupant. Several prepost studies have evaluated the clinical impact of HPV [43,118–120]. For example, Boyce et al. performed a before-after study showing that HPV decontamination of rooms vacated by patients with *C. difficile* infection (CDI) significantly reduced the

Table 15.4 Clinical impact of ARD systems in controlled studies outside of an outbreak setting.

Study	ARD system	Design	Outcome	Confounders
McCord [119]	HPV	4 year before-after	CDI rate fell from 1.0 to 0.4 cases per 1000 pt. days; 60% reduction, $P < .001$.	No data on IPC compliance/ abx use.
Horn [120]	HPV	3 year before-after	CDI, VRE, ESBL and MRSA rate fell significantly.	Concurrent increase in hand hygiene compliance.
Passaretti [13]	HPV	36-month cohort	Pts admitted to rooms decontaminated using HPV 64% less likely to acquire MDRO (IRR = 0.36, CI = 0.19–0.70, $P < .001$).	Not randomized.
Manian [196]	HPV	2 year before-after	CDI rate fell from 0.9 to 0.5 cases per 1000 pt. days; 39% reduction (IRR = 0.63, CI = 0.50–0.79, $P < .001$).	Bleach disinfection enhanced concurrently.
Boyce [43]	HPV	2 year before-after	CDI rate fell from 1.9 to 0.9 cases per 1000 pt. days on high-risk wards; 53% reduction, $P = .047$).	Outbreak? No significant reduction hospital wide; changes in abx usage.
Mitchell [121]	aHP	6 year before-after	MRSA detection from environmental surfaces reduced from 24.7% to 18.8%. Incidence of MRSA acquisition reduced from 9.0 to 5.3 per 10,000 patient days.	Study performed over a long period; changes made in MRSA diagnostic protocols.
Anderson [122]	UVC	Cluster RCT	Significant MDRO acquisition reduction on the hospital level	Monitored potential confounders
Anderson [12]	UVC	Cluster RCT	Significant MDRO acquisition reduction on an individual level	Monitored potential confounders
Pegues [124]	UVC	2 yr before-after	Significant reduction in *C. difficile* compared with control wards	Monitored potential confounders
Napolitano [123]	UVC	3 yr before-after	Significant reduction in the incidence of HAI.	No data on IPC compliance / abx use.
Vianna [73]	PX-UV	4 yr before-after	Significant reductions of *C. difficile* (hospital-wide) and VRE (ICU)	No data on IPC compliance / abx use.

Continued

Table 15.4 Continued

Study	ARD system	Design	Outcome	Confounders
Catalanotti [74]	PX-UV	4 yr before-after	Significant reduction in class I (clean) SSI.	Dedicated housekeeper.
Fornwalt [125]	PX-UV	2 yr before-after	Significant reduction in hip and knee SSIs.	QIP programme including PX-UV.
Miller [197]	PX-UV	3 yr before-after	Significant reduction in *C. difficile*.	Outbreak? Patient management changes.
Haas [126]	PX-UV	4 yr before-after	Significant reduction in HAI.	"Many simultaneous interventions."
Levin [198]	PX-UV	2 yr before-after	Significant reduction in *C. difficile*.	Abx changes.
Simmons [199]	PX-UV	3 yr before-after	Significant reduction in MRSA.	Bundled intervention.

incidence of CDI both on targeted wards and hospital-wide when the analysis was restricted to the months when the epidemic strain was known to be present [43]. McCord et al. [119] reported a significant reduction in CDI associated with the implementation of HPV to augment discharge disinfection protocols in a 4-year prepost study with a 2-year intervention period.

15.5.3.2 H_2O_2 aerosol

One study evaluated the impact of introducing a 6% aHP system on the rate of MRSA acquisition [121]. This before-after study design found that the introduction of aHP reduced MRSA detection from environmental surfaces from 24.7% of rooms following detergent cleaning to 18.8% of rooms after aHP. Also, the incidence of MRSA acquisition reduced from 9.0 to 5.3 per 10,000 patient days in detergent and aHP arms, respectively.

15.5.3.3 UVC systems

A recently published comprehensive cluster randomized controlled intervention trial demonstrated that UVC to augment terminal room disinfection improves patient outcomes by reducing the acquisition of MDROs [12]. The study was performed in 9 hospitals over 2 years and included 31,226 patients. Patients admitted to rooms disinfected using UVC were significantly less likely to acquire MRSA and VRE when admitted to rooms where the previous occupant had these pathogens; there was no significant reduction in *C. difficile* infections. A reanalysis of data from the same study evaluated whole-hospital outcomes, and found a significant reduction in VRE and *C. difficile* [122].

Several before-after studies have shown that adding UVC to disinfection protocols reduces the transmission of MDROs [123,124]. For example, one study reported a significant reduction in *C. difficile* infection in intervention wards compared with control wards in a before-after study design [124].

15.5.3.4 PX-UV systems

A number of studies suggest that the introduction of PX-UV improves patient outcomes [73,74,125]. However, these studies include important and sometimes multiple confounders, making it difficult to determine the impact of PX-UV from other interventions. For example, in one study a dedicated new environmental hygiene staff member was implemented along with PX-UV [74]; in another, PX-UV formed one part of a multifaceted quality improvement program to prevent SSI [125], and in another, “multiple simultaneous interventions” were implemented simultaneously [126].

15.5.4 Practical considerations

15.5.4.1 aHP systems

aHP is straightforward to use and relatively inexpensive compared with H_2O_2 vapor and UVC systems. The capacity of single units to decontaminate areas larger than single rooms is limited so multiple generators may be necessary [81]. Doors and

air vents should be sealed and hand-held health and safety monitors are required to ensure that no leakage occurs during cycles and to verify that the concentration of hydrogen peroxide inside the enclosure is below health and safety exposure limits [82]. Reported cycle times are 3–4 h for multiple cycles [81,96] and 2 h for single cycles [77]. However, cycle times for single rooms may be considerably longer when hand-held sensors are used to ensure the hydrogen peroxide concentrations are below health and safety limits prior to room re-entry [82]. Several studies suggest that homogeneous distribution of the active agent is not achieved [77,81,82], perhaps because aHP is introduced via a unidirectional nozzle and the particles are affected by gravity. Sublethal exposure to hydrogen peroxide or silver could result in the development of tolerance or resistance [50,127,128]. The potential for transferable resistance to silver is greater than for hydrogen peroxide due to plasmid-mediated silver resistance genes [127,128]. Data are required confirming the compatibility of aHP systems with common hospital materials, including sensitive electronics. Finally, several studies have noted equipment reliability problems [77,82,93], which was a feature of older foggers [27].

15.5.4.2 H_2O_2 vapor systems

H_2O_2 vapor systems have been used to decontaminate rooms [39,43], multibedded bays [43,97,114], and entire units [43,69,99]. However, H_2O_2 vapor systems are less straightforward than UV and aHP systems because they require two units (a generator and aeration unit) for a single room. Door and air vents need to be sealed. As with aHP, hand-held health and safety monitors are required to ensure that no leakage occurs during cycles and that the concentration of hydrogen peroxide inside the enclosure is below health and safety exposure limits (1 ppm) before re-entry. Thus, staff training requirements for using hydrogen peroxide systems are higher than for UV systems. The potential for selection of less susceptible strains is lower than for aHP or UV systems because the high concentration H_2O_2 vapor systems ensures that few micro-organisms undergo sublethal exposure. Reported cycle times are currently 1.5–2.5 h for a single room for HPV [129,130] and 8 h for VHP [85]. The compatibility of HPV with hospital materials, including sensitive electronics, is well established [131,132].

15.5.4.3 UV systems

UVC is easy to use, does not require sealing of door or air vents, and has a relatively short cycle time. Many high-touch sites may be out of line of sight; some manufacturers recommended multiple cycles in different parts of the room to overcome this problem but this places reliance on the operator to choose appropriate equipment locations, has implications for cycle times, and requires more hands-on operator time. A recent study indicates that a UVC spore cycle in rooms ranging from 46 to 86 m^3 took a median of 84 min (range 72–146 min) for a two-stage procedure (where the UVC unit is positioned at two locations during the cycle) and a median of 68 min (range 34–100 min) for a one-stage procedure [86]. Since some UVC systems rely on measurement of reflected dose to determine the cycle, the presence of surfaces that do

not reflect UVC, or reflect it inefficiently (such as glass), variations in temperature and humidity and the age of the bulbs will affect the reflected dose and may increase the cycle times [133,134]. The intensity of the UV light dissipates with the square of the distance from the source, which limits the capacity of single UVC devices to disinfect areas larger than single patient rooms [135]. The long-term impact of UVC on hospital materials has not been described [136]. UVC is relatively expensive compared with other ARD systems [137]. Finally, UV radiation is a known mutagen [138]; since UVC systems do not inactivate all microbes in the room, a proportion of those that have received a sublethal dose may undergo mutation.

PX-UV systems have similar practical considerations to UVC systems, including the need to use multiple room locations to address line of sight issues, the age of the bulbs affecting intensity of the pulse, limited capacity to decontaminate areas larger than singe rooms, and the potential for mutagenesis. Also, the system operates using a series of bright "camera flashes," which may be disruptive to patients and staff outside the room.

15.5.5 Other systems

Gaseous ozone for room disinfection has also been evaluated [139,140]. Two studies of different ozone generators were performed in test chambers of 30–35 m^3, which used a concentration of ozone gas peaking at 20–25 ppm. These studies indicated a 3–4 log reduction on vegetative bacteria, a <3-log reduction on mycobacteria, and a dose-dependent <3-log reduction on bacterial endospores in one study [140] but a >4-log spore reduction in the other [139]. Both evaluations tested the systems at high humidity, one at 80%–90% [140] and one at >95% [139]. Another system used a high concentration of gaseous ozone (80 ppm) and up to 3% aerosolized hydrogen peroxide combined with high humidity (80%) to achieve a >6-log reduction of various hospital pathogens in vitro [141]. Substantially lower reductions were achieved at lower relative humidity [141]. The requirement for high humidity is a major practical limitation for ozone-based systems [142]. Furthermore, ozone is toxic to humans, with a safe exposure level in the United Kingdom and United States of <0.1 ppm (compared with 1 ppm for hydrogen peroxide), so effective containment of the gas, monitoring for leakage, and measurements to assure that the room is safe to enter are necessary for these systems in the healthcare setting [143,144]. Data on the compatibility of this process with hospital materials are needed, given ozone's known corrosive properties [17].

Chlorine dioxide has a high level of efficacy against a range of pathogens [93]. However, concerns about safety and material compatibility mean that it is unlikely to be used in healthcare settings [93,132].

"Fogging" with various chemicals, including superoxidized water [145,146], solutions of hydrogen peroxide [147,148], and other chemicals [25,26,149,150], have been evaluated. The efficacy data on a mixture of low-concentration hydrogen peroxide with low concentration peracetic acid are promising, harnessing the natural synergy between these two peroxygen chemicals [151]. These systems are limited by directional introduction of the active agent and consequent nonhomogeneous distribution,

and the potential for the accumulation of large volumes of chemicals that require postprocess removal [148], with associated risks to operators. Data on compatibility with hospital materials are awaited.

15.5.6 Comparing systems

Table 15.5 compares the features of ARD systems.

The performance of different systems can be evaluated by several measures, including compliance with testing standards (such as EN or ASTM standards), in vitro log reduction of bacterial loads, measurement of microbial surface contamination before and after treatment, or by the use of biological indicators (BIs) with a known concentration of a microbe, typically a bacterial endospore. BIs can be produced in-house or, more reliably, can be purchased commercially (typically containing *G. stearothermophilus* bacterial endospores). Most ARD systems produce a more significant reduction of bacterial contamination than conventional disinfection [39,41,77,80,86,87]. However, comparison of the relative effectiveness of different ARD systems is diffi-

Table 15.5 Comparing ARD systems.

	HPV 30%–35% H_2O_2 vapor[a]	**AHP 5%–6% H_2O_2 + Ag aerosol**	**UVC UVC (280 nm)**	**PX-UV Pulsed-xenon UV**
Efficacy	1 >6-log reduction	2 ~4-log reduction[a]	3 ~2–4 log reduction	4 ~1–3 log reduction
Distribution	1 Homogeneous	2 Nonhomogeneous	3 Line of sight issues	3 Line-of-sight issues
Ease of use	4 Multiple units; sealing/ monitoring	3 Sealing & monitoring	2 Multiple positions; no sealing/ monitoring	2 Multiple positions; no sealing/ monitoring
Cycle time	3 ~1.5 h single room	4 >2 h single room	1 ~10–30 min	1 ~10–30 min
Purchase cost	2	1	3	3
Running cost	4	3	1	1

The table subjective ranks the four common classes of ARD systems currently available by their qualities.
[a]Emerging evidence that low concentration hydrogen peroxide/peracetic acid combination can reach similar levels of efficacy to high concentration hydrogen peroxide [151].

cult because of variations in sample sites (especially orientation and proximity to the ARD device), patient infection or colonization status, the organism, the microbiological testing methods, and the type of precleaning. Thus, the best way to compare different systems is through controlled head-to-head studies [71], ideally using clinical infectious or transmission outcomes. However, there have been few studies comparing these outcomes, so it is not possible to evaluate the relative clinical impact of ARD systems using current data. Thus, the available head-to-head studies are currently the most useful way to compare ARD systems.

A recently published study comparing HPV (Bioquell) with an aHP system (ASP Glosair) was performed by St. George's Hospital, London [82]. Testing was performed in a 50 m^3 room with a 13 m^3 anteroom, selected to represent a single occupancy room with a bathroom. Safety was evaluated using a hand-held hydrogen peroxide sensor. The workplace exposure limits (WEL) for hydrogen peroxide are 1 ppm as an 8-h time weighted average, or 2 ppm for 15 min as a short term exposure limit (STEL) [144]. The HPV manufacturer mandates re-entering the room only after the measurable concentration of hydrogen peroxide is <1 ppm; the aHP manufacturer recommended room re-entry 2 h after the start of the cycle. Thus, in this study the mean concentration of hydrogen peroxide in the room was measured 2 h after the cycle started for both systems. The mean hydrogen peroxide concentration in the room 2 h after the cycle started was 2.8 ± 0.8 ppm for aHP, with a maximum reading of 4.5 ppm and no readings <2 ppm, and 1.3 ± 0.4 ppm for HPV, with no readings >2 ppm. Thus, for both systems room re-entry must be controlled by measurements of H_2O_2 concentrations rather than assuming safe levels at the end of the process. A "controlled leakage" experiment was performed in the St George's study to determine whether hydrogen peroxide leaked from an unsealed room door. This was only done for the aHP system because the user manuals recommend door and air vent sealing with adhesive tape for the HPV system but not for the aHP. >20 ppm H_2O_2 was detected outside an unsealed door, indicating that doors must be sealed during cycles. These findings also imply that air vents should be sealed during room disinfection with hydrogen peroxide systems.

Microbiological efficacy was assessed by using commercially available 6-log *G. stearothermophilus* biological indicators and in-house prepared test discs inoculated with MRSA, *A. baumannii*, and *C. difficile* (spores) placed at 11 locations around the room [82]. In addition, in-house prepared test discs dried in three or 10% bovine serum albumin (BSA) to simulate dirty conditions were tested in two further room locations. There are no standard testing methods for ARD systems, so the in-house test discs were used to measure log reductions of the common nosocomial pathogens and 6-log and 4-log *G. stearothermophilus* BIs were used two provide two levels of challenge. HPV inactivated 91% (40/44) of the 6-log and 95% (42/44) of the 4-log *G. stearothermophilus* BIs. HPV generally achieved a 6-log reduction of the MRSA, *A. baumannii*, and *C. difficile* BIs regardless of room location. aHP inactivated 13.6% (6/44) of the 6-log BIs, and 36.4% of the 4-log BIs. aHP achieved a <4-log reduction at 2/11 room locations for MRSA, 7/11 for *A. baumannii* and 2/11 for *C. difficile* spores. The aHP system had reduced efficacy against the catalase-positive *A. baumannii* with a <2-log reductions at 6/11 of room locations. HPV achieved a >5-log reduction at 11/12 locations with MRSA, *A. baumannii*, or *C. difficile* dried in three

or 10% BSA compared with 3/12 locations for aHP. This suggests that HPV is more able to penetrate increasing levels of soil, which may be important with suboptimal precleaning. The log reduction of the in-house prepared test discs varied considerably by room location for aHP but not for HPV, indicating a more uneven distribution of the active agent for aHP.

Another recent head-to-head study was performed in Malmo, Sweden and compared the same HPV and aHP systems. Testing was performed in a 136 m^3 room selected to represent a dual occupancy room. An HPV cycle from a single unit inactivated all 48 6-log *G. stearothermophilus* BIs distributed around the test room [81]. After three back-to-back cycles using two units, 50% of 48 BIs were inactivated by the aHP system. Ninety percent of BIs yielded bacterial growth after the first aHP cycle compared with 21% after both cycles two and three, suggesting poor repeatability. BIs grew in different locations in repeat experiments with the aHP system, suggesting variable distribution. The HPV system was faster than the aHP system, as in the St George's study [82].

The UK Health and Safety Laboratory performed a detailed head-to-head study of six room decontamination technologies including HPV and aHP systems [93]. The microbial challenges (including *C. difficile* spores) were designed to simulate "worst-case" contamination encountered in laboratories. Organisms were dried onto stainless steel discs and exposed to the decontamination processes in a 35 m^3 room and 105 m^3 laboratory. HPV achieved a 5- to 6-log reduction of *C. difficile* spores in all locations apart from in a wet spillage. aHP achieved a <1-log reduction for *C. difficile* spores in all room locations. Both systems were less effective than in other studies, probably because the discs were prepared using growth media that provides an additional level of protection for the microorganisms. These authors recommended that "*All systems should be sold with a device for monitoring fumigant levels at the end of a cycle*."

These results indicate that HPV is faster and more effective for biological inactivation than aHP [81,82,93]. However, the studies reported above were not performed in a clinical setting and did not evaluate surface decontamination directly or the impact on pathogen transmission.

A head-to-head study performed at a US hospital compared HPV (Bioquell) with a UVC system (Tru-D, Lumalier) [152]. In-house prepared carrier disks inoculated with $\sim 10^6$ *C. difficile* spores and BIs with 10^4 and 10^6 *G. stearothermophilus* spores were placed in five sites (3 sites were not in the direct line of sight of the device). UVC achieved a mean of 2.2-log reduction for *C. difficile* (range 1.7–3-log reduction) and inactivated 29% (22/75) of 4-log BIs (range 7–53%) and 0% (0/75) of 6-log BIs. UVC was significantly less effective out of direct line of sight: it inactivated 42% of 4-log *G. stearothermophilus* BIs in direct line of sight but only 7% of 4-log BIs out of direct line of sight. HPV achieved a >6-log reduction for *C. difficile* in all five sites and inactivated 99% (74/75) of 6-log BIs and 100% (75/75) of 4-log BIs. UVC was faster but less effective than HPV for the inactivation of BIs and microbes on surfaces.

A head-to-head study comparing the efficacy of two UVC systems found that their efficacy was not significantly different [153]. However, a separate study found that the efficacy of a UVC system was superior to the efficacy of a PX-UV system when operated for the same amount of time from the same point in the room [112].

15.5.7 Cost

ARD systems can be purchased, rented, or introduced as part of a service contract. These deployment models have different costs, depending on the package and the frequency of use [129].

Several factors must be taken into account when considering the cost of ARD systems. For hospitals that purchase their own ARD system, upfront costs include the equipment itself, staff training (and possibly recruitment), and possibly costs associated with equipment storage. Ongoing costs include personnel costs, consumables (such as hydrogen peroxide or replacement UV bulbs), depreciation, maintenance, and power. For hospitals that choose to purchase a service or other model, manufacturers should be contacted to discuss available options.

Few studies disclose the cost of currently available ARD systems. The Emergency Care Research Institute (ECRI) reports the list price for the Lumalier Tru-D UVC device as £77,190 (US$124,500), the Bioquell HPV system as £27,280 (US$44,000), and the Xenex PX-UV system as £1862 (US$3000) per month over a 36-month lease [137]. Thus, the relative purchase cost of equipment is likely to be UVC > PX-UV > H_2O_2 vapor systems > aHP [137]. Consumables costs for the hydrogen peroxide systems are likely to be greater than the cost of bulb replacement for the UV systems. Manufacturers should be contacted to provide current prices and purchasing options.

No studies of the cost-effectiveness of ARD systems have been published. Performing a cost-effectiveness study on the use of an ARD system should consider the direct and indirect costs associated with the system, any impact on rates of infection with their associated costs and other factors [154].

Several studies have examined the use of ARD systems to disinfect personal protective equipment and other hospital supply items, which could result in financial savings [155,156].

15.6 When to consider an ARD system

Current CDC guidelines recommend against routine "disinfectant fogging" in patient-care areas [28]. This recommendation is currently being re-evaluated by the CDC based on data that have emerged since the guidelines were published and suggest ARD systems may be warranted in some circumstances. The strongest reason for considering an ARD system is to break the chain of transmission by improving terminal disinfection of clinical areas after patients infected or colonized with certain pathogens have been discharged [1,16]. Key pathogens associated with contamination of the environment include *C. difficile*, VRE, MRSA, *A. baumannii*, *P. aeruginosa*, and norovirus [1].

Because of practicality, cost and resource constraints, ARD systems are not suitable for performing disinfection of general clinical areas or daily disinfection of rooms before patients are discharged because of the need for temporary patient relocation. One study evaluated the use of HPV to disinfect the room of a patient colonized with

multiple MDROs [157]. The patient was temporarily relocated and his room decontaminated. Decontamination was effective, but the room was recontaminated shortly after the patient returned. Such recontamination was also seen after HPV decontamination of an ICU [98]. ARD systems have been used to control endemic infection [1,16,43] and outbreaks [69,85,97,99,113–115]. While disinfection of single rooms is more common, ARD systems have been used to disinfect multioccupancy areas, particularly to remove environmental reservoirs during outbreaks [43,69,97,99,114] and whole wards have been disinfected in some studies [43,69,99]. The different indications for the use of ARD systems are outlined in the following scenarios.

15.6.1 Scenarios when the use of an ARD system may be indicated

The choice of whether to rely on current cleaning and disinfection methods enhanced conventional methods or an ARD system will be determined by the clinical scenario. The key factors are whether the area to be disinfected is a single room or a multioccupancy area, whether the clinical setting is high-risk for infection acquisition (e.g., an ICU) or low-risk (e.g., a general ward), and the target organism [13,43,77,80,99]. The risk associated with individual pathogens in the context of disinfection will depend on a number of factors, including the importance of environmental contamination in transmission, clinical implications, local epidemiology, and financial outcomes. For example, a multidrug-resistant Gram-negative rod or *C. difficile* causing an outbreak would be considered a "high-risk" pathogen, whereas VRE colonization would be considered lower risk. Further issues that may need to be considered are the clinical, financial, and reputational effects of environmental infections, especially during on-going outbreaks requiring ward closures. Closures may have particular adverse impacts when they involve specialist regional units such as those for neonatal, pediatric, or adult intensive care.

The disinfection of multioccupancy bays using ARD systems is constrained by the need to accommodate patients elsewhere during the disinfection process [158]. However, this may be necessary and justified to bring a serious outbreak of high-risk pathogens in high-risk patients under control. It may be practical to use UV systems for the disinfection of single rooms used by patients with low-risk pathogens in low-risk settings [87,88] but practical constraints limit the use of hydrogen peroxide ARD systems in this situation. Conversely, H_2O_2 vapor systems would be appropriate for dealing with high-risk pathogens in high-risk units because of their high levels of efficacy, homogeneous distribution, and disinfection assurance [41,43,116]. Examples include on-going outbreaks in intensive care units with NAP1/027 *C. difficile* or a multidrug-resistant Gram-negative pathogen. UV and hydrogen peroxide systems may be suitable for disinfection of single rooms in low-risk settings with high-risk pathogens or in high-risk settings with low-risk pathogens [39,43,77,87,96]. Enhanced conventional disinfection methods should also be employed in these scenarios [8,42,64,65,159,160], with the possible exception of high-risk pathogens occurring in high-risk settings where even enhanced conventional disinfection has been shown to leave residual contamination [8,35,41,42].

Other potential applications of ARD systems include: the removal of environmental pathogens disturbed during building works such as *Aspergillus fumigatus* [161]; as part of emergency preparedness planning [116]; the disinfection of mobile medical equipment in a dedicated facility; and decontamination of emergency vehicles or operating theatres [162]. The widespread need for decontamination of complex mobile medical equipment and furniture, such as blood pressure cuffs, ventilator tubing, wheelchairs, commodes, computers, and other electronics [114,163,164], means that dedicated disinfection rooms incorporating ARD systems are becoming recognized as very useful hospital facilities.

15.7 Using, validating, and regulating ARD systems

15.7.1 The need for precleaning

As with all forms of decontamination, cleaning is required prior to ARD disinfection system in order to remove organic matter that reduces the effectiveness of ARD systems [82,91,103,107,165,166]. The impact of organic matter has been demonstrated by several in vitro studies. For example, Otter et al. evaluated the efficacy of HPV for the inactivation of MRSA dried on stainless steel discs in suspending media containing 0.3%, 3%, and 10% BSA [107]. The effectiveness of HPV was reduced as the concentration of BSA increased. There is evidence that some ARD systems are more susceptible to organic soiling than others. For example, the study by Fu et al. showed that aHP is more susceptible to simulated soiling by BSA than HPV [82].

Nevertheless, several studies demonstrate that ARD systems can produce significant reductions in environmental contamination even without precleaning [39,87,88]. For example, in one study, one site out of 85 sampled yielded MRSA after HPV without precleaning compared with 61 (72%) of 85 matched sites before HPV [39]. In this instance, MRSA was identified by broth enrichment, indicating a low level of contamination, and was cultured from a floor corner that was visibly dirty.

15.7.2 Validation

One of the problems with conventional cleaning and disinfection is the difficulty in validating the processes. The major advantage of ARD systems is the reduction or removal of reliance on the operator to assure adequate distribution and contact time of a disinfectant. It follows that ARD systems should be validated to ensure that their automated processes are effective and repeatable.

ARD systems could be validated by routine microbiological sampling using conventional standards [36], but this is time-consuming, costly, and requires microbiological expertise. Another option is the use of BIs, which provide a semiquantitative measure of microbiological efficacy and repeatability [43,81]. The question remains as to whether 6-log BIs are an appropriate test for validating ARD systems, given that the concentration of contamination on hospital surfaces is usually in the 2-log range [37,81,167]. Walder and Holmdahl [37] argue that soiling and biofilms [168,169],

occasional higher levels of contamination [35], the occurrence of pathogens with reduced susceptibility to certain agents [90], and the potential for incomplete distribution [81,82,152] mean that 6-log BIs are an appropriate target for ARD systems. Recent evidence published by Pottage et al. [90] and others [82,91,93] indicating that catalase-positive bacteria are less susceptible to hydrogen peroxide-based ARD systems than bacterial endospores provides a further reason to use stringent challenges for these systems [167].

The US Environmental Protection Agency (EPA) requires a hospital disinfectant to achieve a >6-log reduction of certain vegetative bacteria in vitro [170]. This is higher than the concentration typically found on hospital surfaces, presumably to provide assurance that the disinfectant will be effective in the "real world."

The inactivation of 6-log BIs correlates well with the elimination of pathogens from surfaces and can be used as a test standard for ARD systems when the elimination of pathogens is required [37,167]. H_2O_2 vapor systems can eliminate pathogens from surfaces, produce a >6-log reduction of a range of pathogens in vitro, and can inactivate 6-log BIs [39,43,91,99]. aHP, UVC, and PX-UV are much less effective in these tests [77,80–83,86–88].

However, further studies are necessary to determine the level of pathogen reduction required to interrupt transmission and set the appropriate clinical decontamination standard for ARD systems.

15.7.3 Regulation

Given the relatively recent introduction of ARD systems into the marketplace, regulatory standards have not been established. In Europe, the regulation of disinfectants is in flux because of the phased introduction of the biocidal products directive (BPD) [171]. Testing standards are generally not specified for ARD systems, although a French standard for testing ARD systems, NF72-281, is currently under evaluation for adoption as a European standard. Currently, it is not clear how the BPD will influence ARD systems, although the ARDs will need to be assessed and registered as with any other disinfectant.

In the United Kingdom, the Health and Safety Executive, Departments of Health (DHs), Health Protection Agencies (HPAs), and various professional societies have a role to play in the regulation of ARD systems. In England, the DH and HPA have established an expert group called the Rapid Review Panel (RRP) to evaluate products claiming to be useful in healthcare applications [129]. The RRP has issued several recommendations on ARD systems. These provide independent, evidence-based recommendations that can guide decision-making about such products. The RRP has issued the following recommendations about ARD systems and are available at http://www.hpa.org.uk/ProductsServices/MicrobiologyPathology/RapidReviewPanel/):

- Bioquell HPV (recommendation 1): Basic research and development, validation, and recent in use evaluations have shown benefits that should be available to NHS bodies to include as appropriate in their cleaning, hygiene, or infection control protocols.
- Steris VHP (recommendation 2): Basic research and development has been completed and the product may have potential value; in use evaluations/trials are now needed in an NHS clinical setting.

- aHP system; Sterinis, now ASP Glosair (recommendation 3): A potentially useful new concept but insufficiently validated; more research and development is required before it is ready for evaluation in practice.

In the United States, the Environmental Protection Agency (EPA) regulates disinfectant use and will likely regulate ARD systems. The EPA issued an order to stop a US hospital using a disinfectant fogger in ambulances on safety grounds [172]. The EPA sought information from some US professional societies and the published open correspondence between the US EPA, Society for Healthcare Epidemiology of America (SHEA), Association for Professionals in Infection Control and Epidemiology (APIC), and Association for the Healthcare Environment (AHE) [173] illustrates that healthcare regulators and professional societies are beginning to take an interest in ARD systems. Similarly, ANSM (previously AFSSAPS), the French regulatory body, has withdrawn several ARD systems, including an aHP system, from the French market due to a lack of efficacy data [174].

Regulators and professional societies will be required to make recommendations on issues such as nomenclature of ARD systems, acceptability of testing standards, and guidance on safe and effective applications. Nomenclature is already confused. For example, the Oxypharm Nocospray aHP system has been incorrectly referred to [75,76] as using “hydrogen peroxide vapor” [78] and correctly as using an aerosol of hydrogen peroxide [72]. Such confusion in describing the various different ARD systems is also evident in several review papers [17,18].

15.8 Sources of further information and advice

Current data on ARD systems in the academic literature are limited but increasing. Academic reviews of ARD systems can provide useful background data, for example, those by Otter et al. [175], Davies et al. [17], and Falagas et al. [18] In addition, publications in the nonpeer-reviewed literature and by research institutes can provide useful background information. For example, the ECRI Institute [137] and Infection Control Today [176] have published useful guidance documents. In addition, several studies of ARD systems with clinical outcomes are currently in progress. Finally, ARD systems increasing are included in certain guidelines as an adjunct to traditional cleaning and disinfection [177,178].

15.9 Future trends

It is likely that the literature evaluating the role of contaminated surfaces in the transmission of nosocomial pathogens will continue to expand. A better understanding of the role of contaminated surfaces in transmission will help to target interventions aimed at improving cleaning and disinfection most effectively. However, at the current time, we do not know the relationship between the level of residual contamination and infection. Ideally, the target should be zero contamination; however, practicalities require a risk-based approach.

Initial studies of systematic improvement of enhanced conventional cleaning methods can reduce transmission to some degree but they often continue to fail because they are dependent on human skill and performance, which cannot be guaranteed. Automated ARD systems are potentially an effective and efficient adjuvant to decontaminating complex environmental surfaces. As the evidence base grows, the indications and cost-effectiveness of ARD systems will become clearer. At present, there is good evidence that terminal disinfection of clinical areas used by patients colonized or infected with pathogens associated with environmental contamination can reduce or eliminate the risk of onward transmission to others, and it is in this situation where ARD systems can be most useful.

The choice of system will depend on practicalities and cost effectiveness. However, more head-to-head comparisons are needed to compare both microbiological and clinical outcomes to allow better evidence-based decision.

Technological developments mean that existing ARD systems will become more refined. For example, improvement in aeration capacity has reduced HPV process times from >4 h [39] to <2 h for a single room [104,130]. Also, the use of UV reflective paint could reduce the impact of line-of-sight issues for UV systems [179]. In addition, there seems to be a natural synergy between the use of ARD systems and self-disinfecting surfaces or air disinfection systems, which can help to reduce the extent of surface contamination during the stay of a patient [180,181]. The emergence of novel ARD systems, combining rapid cycle times with high-level efficacy, would broaden the potential application of ARD systems.

15.10 Conclusions

There is now evidence that existing ARD systems are an effective adjunct to conventional methods of terminal disinfection, and that H_2O_2 vapor and UVC systems reduce transmission in endemic and epidemic settings. Further evidence on the optimal application and cost effectiveness of ARD systems in healthcare is required, but ARD systems are already beginning to be integrated into hospital disinfection policies [13,43]. Regulators and professional bodies should decide on the terminology and insist on standardization for these systems and, as adoption and the evidence-base grows the role of regulators and professional societies will become increasingly important in the provision of advice and guidelines to ensure the safe and effective use of ARD systems in healthcare settings [28,177].

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