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Review

The role of 'no-touch' automated room disinfection systems in infection prevention and control

J.A. Otter [a,b,*], S. Yezli [b], T.M. Perl [c,d], F. Barbut [e], G.L. French [a]

[a] Centre for Clinical Infection and Diagnostics Research (CIDR), Department of Infectious Diseases, King's College London, School of Medicine and Guy's and St Thomas' NHS Foundation Trust, UK
[b] Bioquell UK Ltd, Andover, Hampshire, UK
[c] Division of Infectious Diseases, Department of Medicine, Johns Hopkins University, School of Medicine, Baltimore, MD, USA
[d] Department of Hospital Epidemiology and Infection Control, The Johns Hopkins Hospital, Baltimore, MD, USA
[e] Infection Control Unit, Hôpital Saint Antoine, Assistance Publique-Hôpitaux de Paris, France

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SUMMARY

Background: Surface contamination in hospitals is involved in the transmission of pathogens in a proportion of healthcare-associated infections. Admission to a room previously occupied by a patient colonized or infected with certain nosocomial pathogens increases the risk of acquisition by subsequent occupants; thus, there is a need to improve terminal disinfection of these patient rooms. Conventional disinfection methods may be limited by reliance on the operator to ensure appropriate selection, formulation, distribution and contact time of the agent. These problems can be reduced by the use of 'no-touch' automated room disinfection (NTD) systems.
Aim: To summarize published data related to NTD systems.
Methods: Pubmed searches for relevant articles.
Findings: A number of NTD systems have emerged, which remove or reduce reliance on the operator to ensure distribution, contact time and process repeatability, and aim to improve the level of disinfection and thus mitigate the increased risk from the prior room occupant. Available NTD systems include hydrogen peroxide (H_2O_2) vapour systems, aerosolized hydrogen peroxide (aHP) and ultraviolet radiation. These systems 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 among NTD systems. The choice of NTD system should be influenced by the intended application, the evidence base for effectiveness, practicalities of implementation and cost constraints.
Conclusion: NTD systems are gaining acceptance as a useful tool for infection prevention and control.

Introduction

Contaminated surfaces have been underestimated as a source from which nosocomial transmission can occur.[1–3] Recent studies show that admission to a room previously occupied by a patient with *Clostridium difficile*, vancomycin-resistant enterococci (VRE), meticillin-resistant *Staphylococcus aureus*

* Corresponding author. Address: Bioquell UK Ltd, 52 Royce Close, West Portway, Andover, Hampshire SP10 3TS, UK. Tel.: +44 (0) 1264 835835; fax: +44 (0) 1264 835917.
E-mail address: jon.otter@bioquell.com (J.A. Otter).

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(MRSA), *Acinetobacter baumannii* and *Pseudomonas aeruginosa* increases the risk of acquiring these pathogens for subsequent occupants of the same room by a factor of two or more.[1,4–8] In these circumstances, current terminal cleaning and disinfection following the discharge of patients with these pathogens is inadequate and needs to be improved. The emergence of the 027/NAP1 epidemic strain of *C. difficile* and potentially untreatable multidrug-resistant Gram-negative bacteria that can also survive on surfaces is a further reason to improve environmental decontamination.[9,10]

Effective cleaning and disinfection using conventional methods relies on a human operator to correctly select and formulate an appropriate agent and distribute the agent to all target surfaces for the necessary contact time. Improvement of these conventional methods depends on modification of human behaviour, which is often difficult. The use of novel 'no-touch' automated room disinfection (NTD) systems provides an alternative approach, which removes or reduces reliance on the operator.[11–14] Automated systems have been adopted widely in other areas of healthcare to remove human error. Examples include robotic surgery and many aspects of critical care such as ventilators. 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.[15]

Despite the relatively recent attention, the concept of NTD is not new. A paper was published in 1901 advising on how to disinfect a 'sick-room' through gaseous formaldehyde.[16] In the 1960s, formaldehyde was replaced by aerosolized chemicals such as quaternary ammonium compounds and phenolics due to concerns over toxicity.[17–19] However, advice from the US Centers for Disease Control and Prevention (CDC) since the 1970s is that disinfectant fogging should not be performed routinely in patient-care areas.[19,20] The emergence of several new NTD systems based on either H_2O_2 or ultraviolet (UV) radiation and the increasing recognition of the importance of environmental contamination in transmission suggests that this recommendation should be re-evaluated.[11]

This review presents evidence for the need to improve or augment conventional cleaning and disinfection; considers the targets for hospital disinfection and when use of an NTD system may be appropriate; summarizes and compares evidence relating to the various NTD systems; and discusses the role of regulators and professional societies in guiding evidence-based adoption.

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. It depends on various factors, including the characteristics of the organism involved, patient susceptibility and staff compliance with infection control policies (for example hand hygiene following contact with environmental surfaces).[21–23] The fact that subsequent occupants of a room vacated by a previously colonized or infected patient are at an increased risk of infection indicates that conventional terminal disinfection does not reduce contamination sufficiently to prevent all transmission in these cases.[1,4,6–8] There is some evidence that the extent to which transmission is interrupted is proportional to the level of surface contamination. For example, Lawley *et al.* used an *in vitro* mouse model to show that the degree to which transmission of *C. difficile* was blocked correlated with the $\log_{10}$ reduction of the various disinfectants tested.[24]

The degree of shedding and the infective dose can be used to guide the appropriate target for 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.[1,25,26] For example, stool concentrations of norovirus can reach $>1 \times 10^{12}$ particles per gram and up to 10^5 virus norovirus particles per 30 cm^2 have been identified on hospital surfaces, whereas the infectious dose is 1–100 particles.[1,26,27] 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 and recent discussion surrounding the intended target for hospital disinfection.[28–30]

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 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; a lower standard may be acceptable in lower-risk settings.[28–30]

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 programmes of targeted improvement rarely eradicate pathogens from surfaces.[31–34] Problems associated with both 'product' and 'procedure' contribute to this (Box 1), in particular, the reliance on the operator to repeatedly ensure adequate selection, formulation, distribution and contact time of the agent. For example, a large assessment of conventional cleaning in 36 acute hospitals using fluorescent markers revealed that less than 50% of high-risk objects in hospital rooms were cleaned at patient discharge.[35]

Modifying human behaviour 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 educational campaigns.[5,11,28,35–37]

Monitoring and feedback can improve the frequency of surfaces that are cleaned and reduce the level of environmental contamination and there is some evidence that improving the efficacy of conventional cleaning/disinfection can reduce the acquisition of pathogens.[5,35,38,39,40–42] However, no studies have evaluated the sustainability of such systematic improvements. Indeed, recent evidence indicates that altering the location of fluorescent dye spots reduced the proportion of objects that were cleaned from 90% to approximately 60%.[11]

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, risking damage to materials and presenting health risks for

Box 1
Summary of problems associated with conventional cleaning and disinfection

Problems associated with the cleaning/disinfection products include:

- Infectiveness of some agents against some pathogens; for example, many frequently used hospital disinfectants are not effective against *C. difficile* spores and norovirus.[44,85,134]
- Toxicity to staff or the environment.[44,46]
- Damage to hospital materials and equipment.[44]
- Susceptibility to interference with organic matter on surfaces.[85]
- Potential for biocide/antibiotic cross-resistance.[82]

Problems with cleaning/disinfection procedures include:

- Adequate distribution of the active agent, given the challenges of the complex hospital environment.[35]
- Ensuring correct contact time for the microbial reduction achieved *in vitro*.[134]
- Repeatability of the process depends on the operator.[35]
- Designation of responsibility for various items, particularly complex portable medical equipment.[135]
- Compliance with protocols/policies from an (often) poorly paid, poorly motivated workforce.[136]
- Inadequate training and education of personnel.[136]
- Inadequate time given to do the job properly.[136]
- Insufficient (or non-existent) cleaning prior to disinfection.[85]
- Incorrect formulation of the disinfectant.[82,137]
- Contamination of cleaning solutions/materials.[137,138]
- The effectiveness of conventional cleaning and disinfection is difficult to monitor.[11]

operators may have limited success in removing environmental reservoirs of pathogens.[27,32,33,43–46] NTD systems offer the potential to overcome some of these problems.[12–14]

When to consider an NTD system

Notwithstanding current CDC guidelines recommending against routine 'disinfectant fogging' in patient-care areas, the use of an NTD system may be warranted in some circumstances based on current data.[20] Figure 1 outlines a hierarchical approach to hospital disinfection, identifying areas where NTD systems may be appropriate, and Table I highlights specific scenarios where various NTD systems may be considered. The strongest reason for considering an NTD system is to prevent environment-borne transmission by improving terminal disinfection of clinical areas after infected or colonized patients have been discharged (Figure 1).[1,11] This has been performed in endemic settings or during outbreaks (Table I).[1,11,43,47–53] Whereas the disinfection of single rooms is more common, NTD systems have been used to disinfect multi-occupancy areas.[43,47,49,51,53]

Conversely, NTD systems are not suitable for performing daily disinfection before patients are discharged due to the need for temporary relocation of the patient. Thus, concerns about recontamination by the room occupant after the NTD intervention are not well placed when considering terminal disinfection because although this recontamination may lead to some indirect infection, it does not prevent the chain of infection between consecutive occupants of the same room being broken.[7,21,31,54–56]

Other potential applications of NTD systems include the removal of environmental pathogens disturbed during building works such as *Aspergillus fumigatus*, as part of emergency preparedness planning, the disinfection of mobile medical equipment in a dedicated facility, and decontamination of emergency vehicles or operating theatres.[57–59] Due to the potential for mobile medical equipment, such as blood pressure cuffs and mobile computers to become contaminated, combined with the challenge of disinfecting them effectively, the feasibility and effectiveness of NTD systems for disinfecting these items should be prioritized for evaluation.[49,60,61]

Overview of NTD systems

Several different types of NTD system are currently used in clinical healthcare settings, the most common being aerosolized hydrogen peroxide (aHP) systems (such as ASP Glosair, previously Sterinis, Steris Biogienie and Oxypharm Nocospray), H_2O_2 vapour systems (such as the Bioquell and Steris systems), and ultraviolet C radiation (UVC) systems (such as Lumalier Tru-D).[11–13,62,63] The different characteristics of these three system types are summarized in Table II. A fourth class of NTD system based on pulsed-xenon UV (PX-UV) radiation has emerged relatively recently and with a limited literature so far.[64]

Aerosolized hydrogen peroxide

Technology description

Aerosolized H_2O_2 systems deliver a pressure-generated aerosol. The systems employed most frequently in healthcare use a solution containing 5–6% H_2O_2 and <50 ppm silver.[63,65–68] Aerosolized droplets are introduced into an enclosure via a unidirectional nozzle.[11,62] One manufacturer (ASP Glosair) states a particle size of 8–10 μm whereas another manufacturer (Oxypharm Nocospray) states a smaller particle size of 0.5 μm.[63,69,70] The dose typically recommended for hospital rooms is 6 mL/m^3, although multiple cycles of this dose have been used in several studies.[69,71] Following exposure, the aerosol is left to decompose naturally without any active aeration system.

Microbiological efficacy

Aerosolized H_2O_2 systems have been shown to reduce contamination with *C. difficile* and MRSA on hospital surfaces.[63,67,68,72,73] However, aHP systems have not been shown to eradicate pathogens in clinical practice. For example, one or more positive *C. difficile* culture was collected from 20% of 15 and 50% of 10 rooms studied after an aHP process.[67,73]

One aHP system (ASP Glosair) achieves an ~4-$\log_{10}$ reduction on *C. difficile* spores *in vitro* and has limited capacity to inactivate commercially produced 6-$\log_{10}$ spore biological indicators (BIs).[69,71,73] 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* and the tuberculocidal activity of aHP.[70,74–78] This is likely because catalase-positive bacteria are considerably less susceptible to the 5–6% H_2O_2 aerosol used

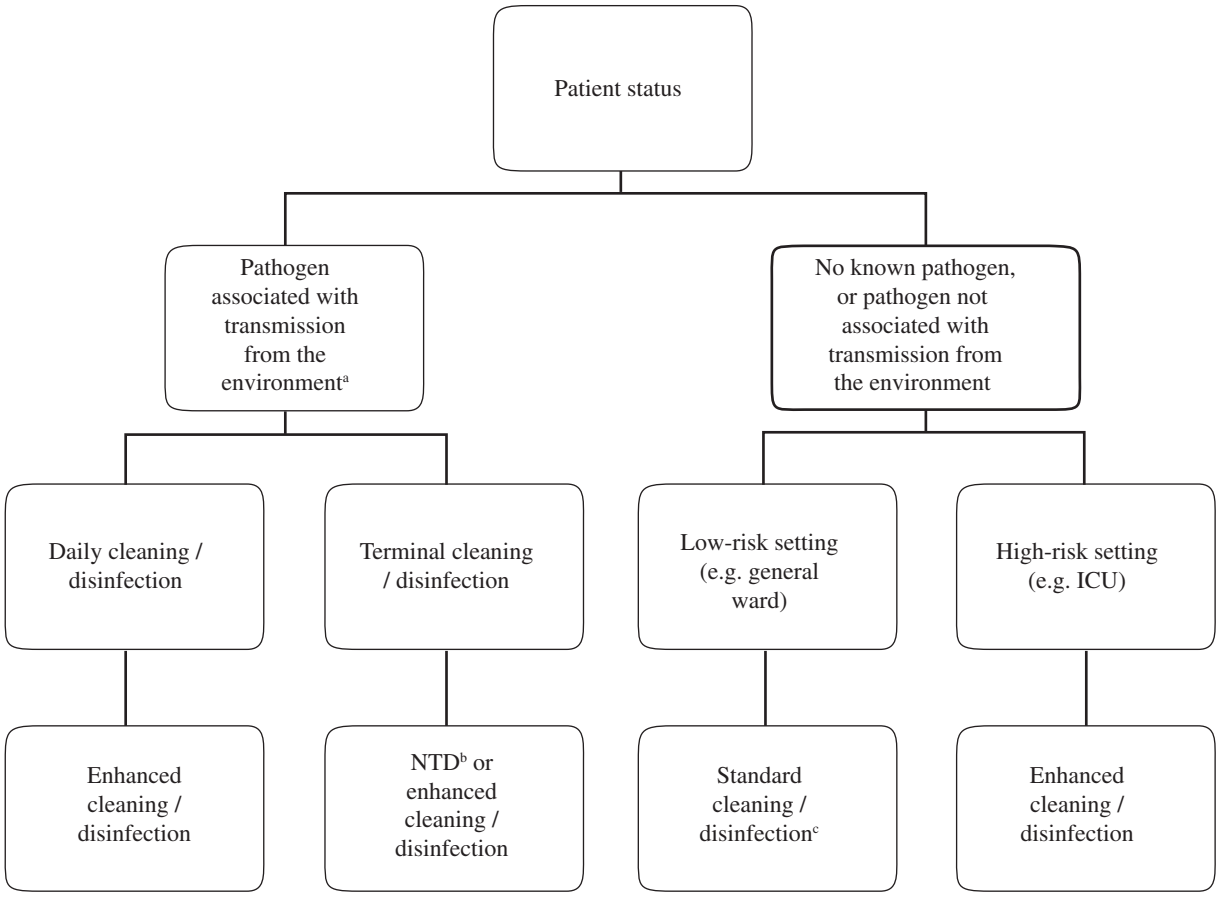

Figure 1. Proposed approach for a disinfection decision diagram. [a]Key pathogens associated with contamination of the environment include *C. difficile*, vancomycin-resistant enterococcus, meticillin-resistant *S. aureus*, *A. baumannii*, *P. aeruginosa* and norovirus. [b]For detailed scenarios when a 'no-touch' automated room disinfection (NTD) system may be considered (Table I). All NTD systems are applied after a cleaning step to ensure that surfaces are free from visible contamination, which is unacceptable to subsequent patients and will reduce the efficacy of the NTD disinfection. [c]There is limited equivocal evidence that enhanced cleaning/disinfection in a low-risk general ward setting can reduce the spread of pathogens.[34,41,141] ICU, intensive care unit.

by aHP systems than catalase-negative bacteria or metabolically inert spores.[79,80]

Clinical impact

There is no published evidence that disinfection with aHP systems reduces epidemic or endemic infection rates.

Practical considerations

Aerosolized H_2O_2 is straightforward to use compared with H_2O_2 vapour systems and relatively inexpensive compared with H_2O_2 vapour and UVC systems. The capacity of single units to decontaminate areas larger than single rooms is limited, so multiple generators may be necessary.[69] 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 H_2O_2 inside the enclosure is below health and safety exposure limits before permitting patients or staff to enter the room.[70] Reported cycle times are 3–4 h for multiple cycles and 2 h for single cycles.[67,69,72] However, cycle times for single rooms may be considerably longer when hand-held sensors are used to ensure that H_2O_2 concentrations are below health and safety limits prior to room re-entry.[70] Some studies suggest that homogeneous distribution of the active agent is not achieved, perhaps because aHP is introduced via a unidirectional nozzle and the particles are affected by gravity, thus being more effective on lower horizontal surfaces.[67,69,70] Sublethal exposure to H_2O_2 or silver could result in the development of tolerance or resistance.[81–83] The potential for transferable resistance to silver is greater than for H_2O_2 due to plasmid-mediated silver resistance genes.[81,83] Data are awaited confirming the compatibility of aHP systems with common hospital materials, including sensitive electronics. Finally, several studies have noted equipment reliability problems, which was a feature of older foggers.[19,67,70,75]

H_2O_2 vapour

Technology description

H_2O_2 vapour systems deliver a heat-generated vapour of 30–35% w/w aqueous H_2O_2 through a high velocity air stream to achieve homogeneous distribution throughout an enclosed area (enclosure).[62,66] Two systems using H_2O_2 vapour are available commercially: Bioquell and Steris (Table II). Bioquell systems

Table I
Detailed scenarios for when to consider a 'no-touch' automated room disinfection (NTD) system for terminal disinfection of clinical areas used by patients infected or colonized with pathogens associated with transmission from the environment

Scenario						Disinfection method		
Single room	Multi-occupancy area	Low-risk settings (e.g. general ward)	High-risk setting (e.g. ICU)	Low-risk environmental—pathogenic characteristics (e.g. VRE/MRSA)[a]	High-risk environmental—pathogenic characteristics (e.g. *C. difficile*)[a]	Standard cleaning and disinfection	Enhanced cleaning and disinfection	NTD[b]
•		•		•		No[31,40]	Yes[41,139]	UVC[100,101]
•		•			•	No[40,140]	Yes[34,141]	UVC[100]/aHP[67]/H_2O_2 vapour[47]
•			•	•		No[39,42]	Yes[5,42]	UVC[100]/aHP[72]/H_2O_2 vapour[31]
•			•		•	No[4,33]	No[27,33]	H_2O_2 vapour[33,47]
	•	•		•	•	No[31,49]	Yes[41,139]	No[c,123]
	•		•	•		No[39,42]	Yes[34,141]	aHP/H_2O_2 vapour[43,49]
	•		•		•	No[4,33]	Unclear[5,34]	H_2O_2 vapour[51]

ICU, intensive care unit; VRE, vancomycin-resistant enterococcus; MRSA, meticillin-resistant *Staphylococcus aureus*; UVC, ultraviolet C spectrum; aHP, aerosolized hydrogen peroxide.
'Yes', method is appropriate based on current data; 'No', method is inappropriate based on current data.
[a] 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 causing an outbreak would be considered a 'high-risk' pathogen, whereas VRE colonization would be considered lower risk.
[b] A cleaning step to ensure that surfaces are free from visible contamination is required before all NTD systems to make the area aesthetically acceptable to the next occupant, and increase the efficacy of NTD disinfection.
[c] The use of an NTD system to disinfect multi-occupancy areas may not be warranted in a low-risk setting due to the requirement to block beds.

are usually termed hydrogen peroxide vapour (HPV) and Steris systems vaporized hydrogen peroxide (VHP). Bioquell HPV includes a generator to produce HPV, modules to measure the concentration of HPV, temperature and relative humidity in the enclosure and an aeration unit to catalyse the breakdown of HPV to oxygen and water vapour 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 H_2O_2 begins to condense on surfaces.[52,84] Steris VHP systems have a generator inside the room with an integral aeration unit and dehumidifier required to achieve a set humidity level prior to the cycle commencement. The system is controlled remotely from outside the enclosure. Steris VHP systems deliver 'non-condensing' VHP by drying the vapour stream as it is returned to the generator. Bioquell systems do not control the H_2O_2 air concentration throughout the exposure period whereas the Steris systems hold a steady H_2O_2 air concentration throughout the exposure period.

Microbiological efficacy

Both Bioquell HPV and Steris VHP systems are US Environmental Protection Agency (EPA)-registered sterilants, which means that they have passed the AOAC sporicide test on porous and non-porous surfaces.[85] Both systems are associated with the eradication of pathogens from surfaces *in situ* and cycles are validated by >6-$\log_{10}$ reduction of *Geobacillus stearothermophilus* BI spores.[33,43,47,51–54,86] HPV and VHP are sporicidal, bactericidal, mycobactericidal and virucidal, achieving >6-$\log_{10}$ reduction against a wide range of nosocomial pathogens including *C. difficile* spores, MRSA, VRE, *A. baumannii* and norovirus surrogates, though efficacy may be reduced by high loading and the presence of organic soil.[70,80,84,87–92]

Clinical impact

HPV has been used to remove environmental reservoirs during outbreaks of *C. difficile*, MRSA and meticillin-susceptible *S. aureus* (MSSA), resistant Gram-negatives and other pathogens.[43,48–51,53,58,86] VHP has been used for the removal of environmental reservoirs during outbreaks of *A. baumannii* in two studies.[52,93] Two pre–post and one cohort study have evaluated the clinical impact of HPV; there are no data for the clinical impact of VHP aside from outbreak settings.[47,94,95] 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 incidence of CDI on five focus wards and hospital-wide, when the analysis was restricted to the months when the epidemic strain was known to be present.[47] A conference abstract by Manian *et al.* showed that HPV decontamination of rooms vacated by patients with a range of pathogens significantly reduced the rate of *C. difficile* and VRE infection, and substantially reduced the rate of MRSA and

Table II
Summary of frequently used 'no-touch' automated room disinfection (NTD) systems

	Aerosolized hydrogen peroxide (aHP)	H_2O_2 vapour	Ultraviolet C (UVC) radiation
Products	ASP Glosair (previously Sterinis)[70] Oxypharm Nocospray[68]	Bioquell HPV systems[70] Steris VHP systems[52]	Lumalier Tru-D[124]
Abbreviation	aHP/'dry mist' HP (DMHP)[66,76]	HPV[70]/VHP[52]	UVC[101]
Active solution	5–6% H_2O_2, <50 ppm Ag cations[69]	30–35% H_2O_2	UVC, 254 nm
Application	Aerosol of active solution	Vapour, either condensing (Bioquell HPV) or non-condensing (Steris VHP)	Radiation
Distribution	Non-homogeneous distribution[63,69]	Homogeneous[69]	Affected by line of sight[99–101]
Particle size	8–10 μm (ASP Glosair)[69,71] 0.5 μm (Oxypharm Nocospray)[63]	Vapour phase	N/A
Process time (single occupancy room)	2–3 h[67,71]	1.5–2.5 h (HPV)[47,90,96,97] 8 h (VHP)[52]	15 min (vegetative setting)[101] 1–1.5 h (spore setting)[99,124]
Required health and safety measures	Air vents and doors isolated; active monitoring with a hand-held sensor necessary to check for leaks and ensure room is safe to re-enter.[70,75]	Air vents and doors isolated; active monitoring with a hand-held sensor necessary to check for leaks and ensure room is safe to re-enter.[31,47]	Air vents and doors not isolated. No requirement for active monitoring or testing to ensure room is safe to re-enter.
Aeration (removal of active solution from enclosure)	Passive decomposition	Active catalytic conversion	Not required
Sporicidal efficacy	Incomplete inactivation *in situ*[67,73]; ~4-$\log_{10}$ reduction of *C. difficile in vitro*; limited ability to inactivate 6-$\log_{10}$ BIs[69–71]	Complete inactivation *in situ*[47]; >6-$\log_{10}$ reduction of *C. difficile in vitro*[80]; routinely validated using 6-$\log_{10}$ BIs[47,69,70]	No studies *in situ*. 1–4-$\log_{10}$ reduction *in vitro* depending on line of sight[99–101]; does not inactivate 6-$\log_{10}$ BIs[124]
Tuberculocidal efficacy	Unclear[75–78]	Yes[75,84,142]	Unclear
UK Rapid Review Panel Recommendation	3: 'A potentially useful new concept but insufficiently validated; more research and development is required before it is ready for evaluation in practice.'	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.' (HPV)	None
EPA registration	Unknown	Sterilant	Unknown
Evidence of clinical impact	None published	Significant reduction in the incidence of *C. difficile* and VRE. (HPV)[47,94,95] Removal of environmental reservoirs during outbreaks.[43,49,51,53,86]	Short duration study indicating a reduction in CDI associated with UVC.[102]

N/A, not applicable; BI, biological indicator; NHS, National Health Service (UK); EPA, Environmental Protection Agency (USA); VRE, vancomycin-resistant enterococcus; CDI, *Clostridium difficile* infection.

multidrug-resistant *A. baumannii* infection.[94] A cohort study by Passaretti *et al.* found 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 rooms vacated by patients with MDROs and disinfected using standard methods.[95] Thus, HPV decontamination successfully mitigates the risk from the prior room occupant.[95]

Practical considerations

H_2O_2 vapour systems have been used to decontaminate rooms, multi-bedded bays and entire units.[31,43,47,49,51,53] However, HPV is less straightforward than UVC and aHP systems because it requires 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 to verify that the

concentration of H_2O_2 inside the enclosure is below health and safety exposure limits before permitting patients or staff to enter the room. Thus, staff training requirements for using H_2O_2 vapour 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 vapour systems typically eradicate pathogens so that few micro-organisms undergo sublethal exposure. Reported cycle times are currently 1.5–2.5 h for a single room for HPV and 8 h for VHP.[52,90,96,97] The compatibility of HPV with hospital materials, including sensitive electronics, is well established.[98]

Ultraviolet C radiation (UVC)

Technology description

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.[99–101] The device is placed in the centre of the room and frequently touched mobile items are arranged close to the device for optimal exposure. UVC travels in straight lines and is less effective out of direct line of sight from the device. Some manufacturers therefore recommend multiple cycles from different locations.[99] 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.

Microbiological efficacy

Several studies of one UVC system (Lumalier Tru-D) indicate a significant reduction of surface contamination.[99–101] However, these reports indicate incomplete inactivation of *C. difficile*, VRE, *Acinetobacter* or MRSA from hospital surfaces.[99–101]

UVC produces a dose-dependent 2–4-log$_{10}$ reduction on nosocomial pathogens experimentally dried on to surfaces.[99–101] It may be possible to improve efficacy at the cost of extending cycles. Importantly, the microbiological reduction is significantly lower out of direct line of sight of the device.[99–101] For example, in one study of a UVC device, a 1-log$_{10}$ reduction was achieved on *C. difficile* spores inoculated on plastic carriers placed 10 feet away from the device out of direct line of sight, compared with 2.6-log$_{10}$ reduction in direct line of sight.[100]

Clinical impact

A recent conference abstract indicates an association between the use of UVC and a reduction in the incidence of CDI.[102] Further clinical studies on this and other pathogens are needed to assess the potential role of UVC systems in reducing nosocomial infection rates.

Practical considerations

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) for a two-stage procedure (where the UVC unit is positioned at two locations during the cycle) and median of 68 min (range: 34–100) for a one-stage procedure.[99] 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.[103,104] UVC is relatively expensive compared with other NTD systems.[105] The intensity of the UV light dissipates with the square of the distance from the source, which limits the capacity of UVC devices to disinfect areas larger than single patient rooms.[106] The long-term impact of UVC on hospital materials has not been described.[107] Finally, UV radiation is a known mutagen.[108] Since UVC systems do not inactivate all microbes in the room, a proportion of those that have received a sublethal dose may undergo mutation.

Pulsed-xenon ultraviolet (PX-UV)

Technology description

Pulsed-xenon ultraviolet systems emit broad spectrum UV in short pulses.[64] They are placed at multiple room locations and have a relatively short cycle time.

Microbiological efficacy

One PX-UV system (Xenex) achieved a significant reduction in VRE contamination in a room in a 12 min cycle.[64] Further efficacy data are awaited.

Clinical impact

A recent conference abstract indicates that the use of PX-UV may be associated with a reduction in the incidence of CDI.[109] However, the study was performed for a short duration so further data are awaited.

Practical considerations

Pulsed-xenon ultraviolet 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 single rooms and the potential for mutagenesis. Also, the system operates using a series of bright 'camera flashes', which may be disruptive to patients. However, given the short cycles associated with PX-UV, it should be prioritized for further evaluation.

Other systems

Gaseous ozone can achieve a high level of microbial inactivation.[110,111] However, the requirement for high humidity is a practical limitation.[112] Furthermore, ozone is toxic to humans, with a safe exposure level in the UK and USA of $<$0.1 ppm (compared with 1 ppm for H_2O_2), so effective containment of the gas, monitoring for leakage and assessing safe levels for re-entry are necessary in healthcare settings.[113,114] Data on the compatibility of this process with hospital materials are needed due to ozone's known corrosive properties.[12]

Chlorine dioxide has a high level of efficacy against a range of pathogens.[75] However, concerns about safety and material

compatibility mean that it is unlikely to be used in healthcare settings.[75,98]

'Fogging' with various chemicals, including super-oxidized water and solutions of H_2O_2 mixed with other chemicals, has been evaluated.[17,18,115–120] These systems are limited by directional introduction of the active agent and consequent non-homogeneous distribution, and the potential for the accumulation of large volumes of chemicals that require post-process removal, with associated risks to operators.[118] Data on compatibility with hospital materials are awaited.

Selecting, validating and regulating NTD systems

The need for pre-cleaning

All NTD systems require cleaning prior to their application ('pre-cleaning') for two reasons: to make the room aesthetically acceptable to the next occupant and to remove organic matter that reduces the effectiveness of NTD systems.[70,80,89,92,121,122] There is evidence from *in vitro* studies that some NTD systems are more susceptible to organic soiling than others. For example, H_2O_2 vapour systems are more able to penetrate increasing levels of organic soiling than aHP.[70,75] However, few studies have evaluated how the level of pre-cleaning influences the efficacy of NTD systems *in situ*. One study of HPV and one study of UVC demonstrated significant reductions on pathogen contamination when the NTD systems were applied without pre-cleaning, suggesting that pre-cleaning protocols could be truncated.[31,101]

The thoroughness of pre-cleaning will have implications for overall process time and cost-effectiveness. One study recorded the time taken for each stage of the HPV room disinfection process.[123] Pre-cleaning of all surfaces in the room using detergent took a median of 24 min. The time taken for pre-cleaning should be accounted for to obtain an accurate NTD room disinfection process time. Reductions in the time taken for pre-cleaning without compromising NTD efficacy may be possible, but further work is required to optimize pre-cleaning protocols for the various NTD systems.

Comparing systems

The performance of different systems can be evaluated by many different measures, including *in vitro* $\log_{10}$ reduction, compliance with testing standards, measurement of microbial surface contamination before and after the process or the use of BIs with a known concentration of a microbe, typically a bacterial endospore. Most NTD systems produce a significant reduction of bacterial contamination compared with conventional disinfection.[31,33,67,73,99,100] However, comparison of the relative impact of different NTD systems is difficult because of variations in sample sites (especially orientation and proximity to the NTD device), patient infection or colonization status, the organism, the microbiological testing methods and the type of pre-cleaning. Thus, the best way to compare the relative efficacy of different systems, however measured, is through controlled head-to-head studies.[62]

A recently published study compared HPV (Bioquell) with an aHP system (ASP Glosair).[70] Testing was performed in a 50 m^3 room with a 13 m^3 anteroom, representing a single occupancy room with bathroom. For both systems it was found that rooms must be sealed to prevent leakage and room re-entry must be led by a hand-held sensor to ensure safety. HPV generally achieved a 6-$\log_{10}$ reduction of spore BIs and in-house-prepared test discs inoculated with MRSA, *C. difficile* spores and *A. baumannii*, whereas aHP generally achieved $\leq$4-$\log_{10}$ reduction. The aHP system had reduced efficacy against the catalase-positive *A. baumannii* with a $<$2-$\log_{10}$ reduction in the majority of room locations. Uneven distribution of the active agent within the enclosure was evident for aHP but not for HPV.

In another recent study comparing the same HPV and aHP systems, an HPV cycle from a single unit inactivated all 6-$\log_{10}$ BIs distributed around a 136 m^3 dual occupancy room.[69] After three back-to-back cycles using two units, 50% of 48 BIs were inactivated by the aHP system. BIs grew in different locations in repeat experiments with the aHP system, suggesting variable and incomplete distribution. The HPV system was faster than the aHP system, as in the study by Fu *et al.*[70]

These results indicate that HPV is faster and more effective for biological inactivation than aHP.[69,70,75] However, these studies were not performed in a clinical setting and did not evaluate surface decontamination directly or impact on pathogen transmission.

A head-to-head study compared HPV (Bioquell) with a UVC system (Tru-D, Lumalier).[124] The UVC system was less effective at reducing the number of sites with bacterial contamination and was affected by line of sight. It inactivated 42% of 4-$\log_{10}$ *G. stearothermophilus* BIs in direct line of sight but only 7% of 4-$\log_{10}$ BIs out of direct line of sight. It inactivated none of the 6-$\log_{10}$ BIs compared with 99% inactivation of 6-$\log_{10}$ BIs and all 4-$\log_{10}$ BIs for the HPV system. In-house prepared discs experimentally contaminated with *C. difficile* spores showed a $>$6-$\log_{10}$ reduction by HPV at all locations and a 1–3-$\log_{10}$ reduction depending on sample location for UVC. UVC was faster but less effective than HPV for the inactivation of BIs and microbes on surfaces.

No head-to-head studies comparing aHP and UVC have been published. More head-to-head evaluations of NTD systems are required, including assessment of relative clinical impact.

Criteria for selecting systems

Typically, there is a trade-off between cycle time and effectiveness among NTD systems. The choice of NTD system should be decided by the intended application. For example, it is doubtful whether the risk of infection and severity of outcome associated with a lower-risk pathogen on a general ward would warrant the increased downtime associated with H_2O_2 vapour or aHP systems, whereas the quicker UV systems may be appropriate (Table I). At the other end of the spectrum, where the risk and severity profile is high, such as NAP1/027 *C. difficile* or a multidrug-resistant Gram-negative pathogen on an ICU, the additional downtime associated with H_2O_2 vapour systems over UV systems may be justified by the higher level of efficacy, homogeneous distribution and disinfection assurance provided by H_2O_2 vapour systems (Table I). It is therefore likely that, as with liquid hospital disinfectants where more challenging standards are applied for tuberculocidal and sporicidal activity, hospitals will select NTD systems according to their infection control priorities and requirements.[85]

Cost

Several factors must be taken into account when considering the cost of NTD systems. First is the question of whether the system will be owned and operated by the hospital, or whether the NTD system will be delivered as a service. Alternatively, leasing is an option that can avoid high capital costs. If the decision is made to purchase an NTD 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 H_2O_2 or replacement UV bulbs), depreciation, maintenance and power. There are few studies disclosing the cost, or evaluating the cost-effectiveness of NTD systems, which will be affected by the degree to which they reduce transmission. The relative purchase cost of equipment is likely to be UVC > PX-UV > H_2O_2 vapour systems > aHP.[105] Consumables costs for the H_2O_2 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.

Validation

The major advantage of NTD systems is the reduction or removal of reliance on the operator to assure adequate distribution and contact time. Thus, validation of NTD systems is desirable to ensure that these automated processes are effective and repeatable.

Routine microbiological sampling to validate NTD systems is time-consuming, costly and requires microbiological expertise. Another option is the use of BIs, which provide a semi-quantitative measure of microbiological efficacy and repeatability.[47,69] Recent discussion has centred around whether 6-$\log_{10}$ BIs are an appropriate test for validating NTD systems, given that the concentration of contamination on hospital surfaces is usually in the 2-$\log_{10}$ range.[29,69,125] Walder and Holmdahl[29] argue that soiling and biofilms,[126,127] occasional higher levels of contamination,[27] the occurrence of pathogens with reduced susceptibility to certain agents[79] and the potential for incomplete distribution[69,70,124] mean that 6-$\log_{10}$ BIs are an appropriate target for NTD systems. Recent evidence published by Pottage *et al.* and others indicating that catalase-positive bacteria are less susceptible to H_2O_2-based NTD systems than bacterial endospores provides a further reason to use stringent challenges for these systems.[70,75,79,80,125]

There is a parallel with standards for liquid hospital disinfectants. For example, the EPA requires a hospital disinfectant to achieve a >6-$\log_{10}$ reduction of certain vegetative bacteria *in vitro*.[128] 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'.

H_2O_2 vapour systems are associated with the elimination of pathogens from surfaces, a >6-$\log_{10}$ reduction of a range of pathogens *in vitro* and the inactivation of 6-$\log_{10}$ BIs.[31,47,51,80] Aerosolized H_2O_2 and UVC do not consistently eliminate pathogens, achieve a <6-$\log_{10}$ reduction *in vitro* and cannot reliably inactivate 6- or 4-$\log_{10}$ BIs.[67,69–71,73,99–101] Therefore, the inactivation of 6-log BIs correlates well with the elimination of pathogens from surfaces and can be used as a test standard for NTD systems when the elimination of pathogens is required.[29,125] However, further studies are necessary to determine the level of reduction required to interrupt transmission in various settings.

Regulation

The open correspondence between the EPA and Society for Healthcare Epidemiology of America (SHEA), Association for Professionals in Infection Control and Epidemiology (APIC) and Association for the Healthcare Environment (AHE) illustrates that healthcare regulators and professional societies are beginning to take an interest in NTD systems.[129] Further, in early 2011, the EPA issued an order to stop a US hospital using a disinfectant fogger in ambulances on safety grounds.[130] Similarly, ANSM (formerly AFSSAPS), the French regulatory body, has withdrawn several NTD systems, including several aHP systems, from the French market due to a lack of efficacy data.[131]

In Europe, the regulation of disinfectants is in flux because of the phased introduction of the biocidal products directive (BPD).[132] Testing standards are generally not specified for NTD systems, although a French standard that has been developed specifically for testing NTD systems, NF72-281, is currently under evaluation for adoption as a European testing standard. Currently, it is not clear how the BPD will influence NTD systems, although they will need to be assessed and registered as with any other disinfectant. In the UK, the government has established a group of experts called the Rapid Review Panel (RRP) to evaluate products claiming to be useful in healthcare applications.[96] The RRP has issued several recommendations on NTD systems (Table II). These provide independent, evidence-based recommendations that can guide decision-making.

Clear nomenclature will be crucial as the NTD market grows, but is already confused. For example, the Oxypharm Nocospray aHP system has recently been termed incorrectly[65,66] as 'hydrogen peroxide vapour'[68] and correctly as an aerosol of H_2O_2.[63] Independent regulators or professional societies should provide a framework for classifying NTD systems.

Due to the number of NTD systems already on the market and the likelihood that more will emerge in the coming years, regulators and professional societies will be required to make recommendations on issues such as nomenclature, acceptability of testing standards and guidance on safe and effective applications.

Conclusion

We do not yet know the relationship between the level of residual contamination and infection. Ideally the target should be zero contamination; however, practicality requires a risk-based approach. More studies are required to determine how far systematic improvement of conventional methods can go in reducing transmission, and to evaluate the sustainability of these improvements. However, conventional methods have inherent limitations that may be overcome through the use of an NTD system.

Strong evidence now exists that the level of terminal disinfection of clinical areas used by patients with pathogens associated with transmission from the environment should be increased in order to prevent environment-borne transmission between patients, and it is in this situation where NTD systems are most strongly indicated. After the decision has been made

to use an NTD system, the choice between systems will depend on balancing the practicalities of the systems, including cost, with the combined risk profile of the pathogen and the hospital unit. Other applications of NTD systems, for example use in operating rooms, emergency vehicles and in primary care facilities, warrant exploration.

There is now evidence that NTD systems are an effective adjunct to conventional methods of terminal disinfection, and that H_2O_2 vapour systems reduce transmission in endemic and epidemic settings. However, the cost-effectiveness of interventions using NTD systems requires further evaluation. More head-to-head comparisons of NTD systems, ideally including comparisons with conventional cleaning and disinfection and assessing both microbiological and clinical outcomes, are required. Such results will reduce reliance on manufacturer claims and expert opinion and allow evidence-based decision-making.

Although further data are required to evaluate the applicability and cost-effectiveness of NTD systems in healthcare, it is likely that NTD systems will form a part of infection control in the future. Regulators and professional bodies should decide on the terminology for these systems and, as the evidence base grows, provide guidelines for their safe and effective use in healthcare settings.[20,133]

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