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A guide to no-touch automated room disinfection (NTD) systems

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Abstract: Conventional disinfection methods are limited by reliance on the operator to ensure appropriate selection, formulation, distribution and contact time of the agent. 'No-touch' automated room disinfection (NTD) systems remove or reduce reliance on operators and so they have the potential to improve the efficacy of terminal disinfection. The most commonly used systems are hydrogen peroxide vapour (H_2O_2 vapour), aerosolised hydrogen peroxide (aHP) and ultraviolet (UV) radiation. These systems have important differences in their active agent, delivery mechanism, efficacy, process time and ease of use. The choice of NTD system should be influenced by the intended application, the evidence base for effectiveness, practicalities of implementation and cost constraints.

Key words: aerosolised hydrogen peroxide, hydrogen peroxide vapour, ultraviolet light, disinfection, gaseous decontamination.

17.1 Introduction

As the role of contaminated surfaces in the transmission of nosocomial pathogens is increasingly recognised, there has been renewed emphasis on the importance of effective cleaning and disinfection (Dancer, 2009; Otter *et al.*, 2011). This chapter considers the rationale for 'no-touch' automated room disinfection (NTD) 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 NTD systems. This chapter provides

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a detailed overview of the four classes of NTD system that are most commonly used in healthcare settings: aerosolised hydrogen peroxide (aHP), (H_2O_2) vapour, ultraviolet C radiation (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 NTD systems and a consideration of their comparative effectiveness and cost. Based on these differences, the scenarios in which various NTD systems may be indicated are discussed in detail. Finally, future trends are also considered.

17.2 Reasons to consider a no-touch automated room disinfection (NTD) system

At one time, contaminated surfaces were thought to contribute negligibly to endemic transmission of pathogens in hospitals (Maki *et al*., 1982; McGowan, 1981). However, recent data indicate that contaminated surfaces make an important contribution to the endemic transmission of certain nosocomial pathogens (Maki *et al*., 1982; Otter *et al*., 2011; Weber *et al*., 2010). The most convincing evidence comes from studies showing that admission to a room previously occupied by a patient colonised or infected with certain pathogens increases the risk of subsequent occupants acquiring these pathogens by a factor of at least two (Datta *et al*., 2011; Drees *et al*., 2008; Huang *et al*., 2006; Nseir *et al*., 2011; Otter *et al*., 2011; Shaughnessy *et al*., 2011). This association has been demonstrated for *Clostridium difficile*, vancomycin-resistant enterococci (VRE), meticillin-resistant *Staphylococcus aureus* (MRSA), *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (Drees *et al*., 2008; Huang *et al*., 2006; Nseir *et al*., 2011; Otter *et al*., 2011; Shaughnessy *et al*., 2011). The epidemiological association is strengthened by the finding that improving terminal room disinfection reduces or eliminates this increased risk (Datta *et al*., 2011; Passaretti *et al*., 2013). 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 hospitalised 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 (Dubberke *et al*., 2007; Peleg and Hooper, 2010).

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 behaviour, which is difficult to achieve and sustain. The use of NTD systems provides an adjunctive approach, which removes or reduces reliance on the operator (Byrns and Fuller, 2011; Davies *et al*., 2011; Falagas *et al*., 2011; Rutala and Weber, 2011).

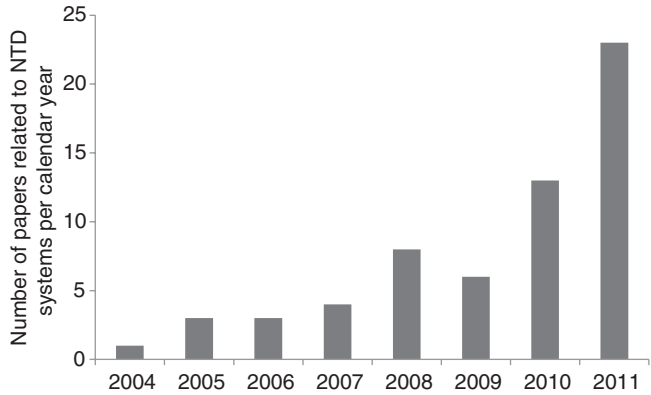
Automated systems have been adopted widely in other areas of healthcare to reduce reliance on operators and mitigate the potential for human error. Examples include robotic surgery and many aspects of critical care such as ventilators (Bryant, 1967; Howe and Matsuoka, 1999). Indeed, commenting on the 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' (Weinstein, 1998). In recognition of these potential benefits, publications about NTD systems have increased sharply in the last two years (Fig. 17.1).

Despite this recent interest, the concept of NTD is not new. Even before germ theory was formulated, 'fumigation' was performed through burning sulphur and other chemical mixtures (Blancou, 1995). A paper published in 1901 provided a step-by-step guide on how to disinfect a 'sick-room' through gaseous formaldehyde (Riddle, 1901). In the 1960s, formaldehyde was replaced by aerosolised chemicals such as quaternary ammonium compounds and phenolics due to concerns over toxicity and provided promising data on effectiveness (Friedman *et al*., 1968; Munster and Ostrander, 1974; Ostrander and Griffith, 1964). 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 (Munster and Ostrander, 1974; Rutala *et al*., 2008). The increasing recognition of the importance of environmental contamination in transmission has prompted the development of several new NTD systems based on either hydrogen peroxide or ultraviolet radiation. The improved efficacy and safety of these systems compared with the disinfectant aerosolisers of the 1960s and 1970s has prompted a re-evaluation of the CDC recommendation (Rutala and Weber, 2011).

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

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

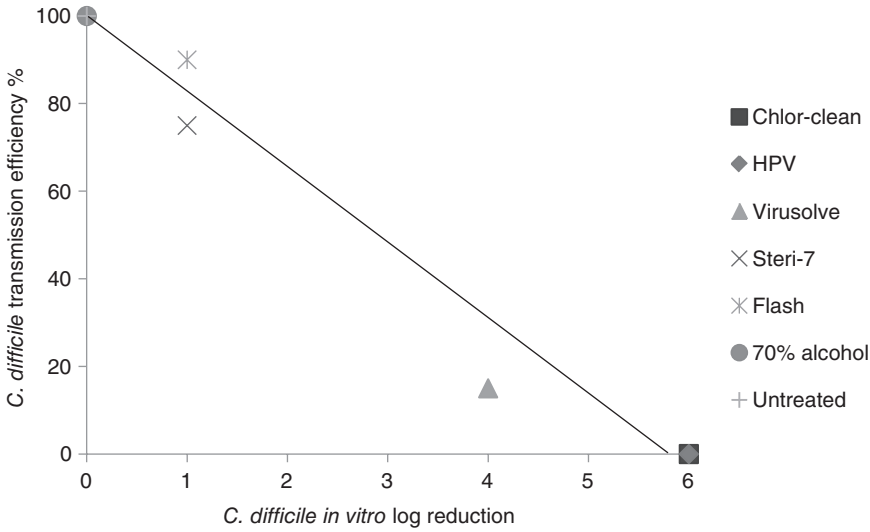
The relationship between the level of residual surface contamination after disinfection and the risk of transmission has not been studied in detail. The



17.1 Pubmed referenced publications relating to healthcare applications of NTD systems since 2004.

2004 (French *et al.*, 2004)
2005 (Jeanes *et al.*, 2005; Bates and Pearse, 2005; Taneja *et al.*, 2005)
2006 (Otter *et al.*, 2006; Clark *et al.*, 2006; McDonnell, 2006)
2007 (Hardy *et al.*, 2007; Hall *et al.*, 2007; Otter *et al.*, 2007; Boyce, 2007)
2008 (Dryden *et al.*, 2008; Boyce *et al.*, 2008; Hall *et al.*, 2008; Shapey *et al.*, 2008; Bartels *et al.*, 2008; Grare *et al.*, 2008; Sharma and Hudson, 2008; Orlando *et al.*, 2008)
2009 (Otter and French, 2009; Otter *et al.*, 2009a, 2009b; Boyce, 2009; Barbut *et al.*, 2009; Moat *et al.*, 2009)
2010 (Otter *et al.*, 2010a, 2010b, 2010c; Pottage *et al.*, 2010; Bergman *et al.*, 2010; Lawley *et al.*, 2010; Po and Carling, 2010; Otter and Yezli, 2010; Andersen *et al.*, 2010; Rutala *et al.*, 2010; Nerandzic *et al.*, 2010; Ray *et al.*, 2010; Callahan *et al.*, 2010)
2011 (Cooper *et al.*, 2011; Berrie *et al.*, 2011; Holmdahl *et al.*, 2011; Manian *et al.*, 2011; Rutala and Weber, 2011; Falagas *et al.*, 2011; Davies *et al.*, 2011; Byrns and Fuller, 2011; Otter and Yezli, 2011; Andersen, 2011; Piskin *et al.*, 2011; Boyce *et al.*, 2011; Stibich *et al.*, 2011; Zoutman *et al.*, 2011; Taneja *et al.*, 2011; Chan *et al.*, 2011; De Lorenzi *et al.*, 2011)
2012 (Pottage *et al.*, 2012; Galvin *et al.*, 2012; Tuladhar *et al.*, 2012; Bentley *et al.*, 2012; Beswick *et al.*, 2011)

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) (Hayden *et al.*, 2008; Kramer *et al.*, 2006; Stiefel *et al.*, 2011). The fact that subsequent occupants of a room vacated by a previously colonised or infected patient are at increased risk of infection indicates that conventional terminal cleaning and disinfection do not reduce contamination sufficiently



17.2 Correlation between *in vitro* log reduction and interruption of transmission of *C. difficile* spores in a murine model (data from Lawley *et al.* (2010)). HPV = hydrogen peroxide vapour.

to prevent transmission in these cases (Drees *et al.*, 2008; Huang *et al.*, 2006; Nseir *et al.*, 2011; Otter *et al.*, 2011; Shaughnessy *et al.*, 2011).

There is some limited evidence that the risk of transmission is proportional to the level of surface contamination. Lawley *et al.* (2010) 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 one 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. 17.2). 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 (Larson and Borriello, 1990; Otter *et al*., 2011; Yezli and Otter, 2011). For example, the infectious dose for norovirus is 1–100 viral particles (Yezli and Otter, 2011) while stool concentrations can reach more than 10^{12} particles per gram (Otter *et al*., 2011) and up to 10^5 norovirus particles per 30 cm^2 have been identified on hospital surfaces (Morter *et al*., 2011). 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 (Dancer, 2004) and recent discussion surrounding the intended target for hospital disinfection (Roberts, 2012; Walder and Holmdahl, 2012).

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 whereas a lower standard may be acceptable in lower-risk settings (Dancer, 2004; Roberts, 2012; Walder and Holmdahl, 2012).

17.4 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 programmes of targeted improvement rarely eliminate pathogens from surfaces (Byers *et al*., 1998; French *et al*., 2004; Manian *et al*., 2011; Wilcox *et al*., 2003). For example, MRSA was identified on 66% of surfaces in patient rooms following terminal cleaning in one study (French *et al*., 2004) and *C. difficile* spores persisted despite bleach disinfection in another (Boyce *et al*., 2008; Kaatz *et al*., 1988; Verity *et al*., 2001).

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 (Fraise, 2011; Humphreys, 2011) and norovirus (Dettenkofer and Block, 2005); toxicity to staff or the environment; damage to materials and equipment resulting in restrictions on usage (Dettenkofer and Block, 2005; Mirabelli *et al*., 2007); certain agents are inhibited by organic matter on surfaces (Humphreys, 2011); and there is a potential for biocide/antibiotic cross-resistance for some agents (Meyer and Cookson, 2010).

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 (Carling *et al*., 2008; Fraise, 2011). 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 (Carling *et al*., 2008). Distribution of the active agent is difficult in the complex and intricate healthcare environment (Carling *et al*., 2008). Ensuring the correct contact time to attain the microbial reduction achieved *in vitro* is particularly problematic because the disinfectant will evaporate from the surface (Fraise, 2011). Other problems include the delegation of responsibility for cleaning, which can fall between staff groups such as nurses and domestic housekeepers particularly in the case of complex portable medical equipment (Havill *et al*., 2011); difficulties in measuring the effectiveness of cleaning and disinfection (Rutala and Weber, 2011) and achieving compliance with protocols/policies from an (often) poorly paid, poorly motivated workforce who may have limited spoken or written local language skills (Dancer, 1999); inadequate training and education of personnel (Dancer, 1999); inadequate time given to do the job properly (Dancer, 1999); insufficient (or non-existent) cleaning prior to disinfection (Humphreys, 2011); incorrect formulation of the disinfectant (Meyer and Cookson, 2010; Weber *et al*., 2007); and contamination of cleaning solutions/materials (Weber *et al*., 2007; Werry *et al*., 1988).

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 education to enhance knowledge about the importance of the process (Boyce *et al*., 2009; Carling *et al*., 2008; Dancer, 2004; Datta *et al*., 2011; Mulvey *et al*., 2011; Rutala and Weber, 2011). 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 (Carling *et al*., 2006, 2008) and reduce the level of environmental contamination (Eckstein *et al*., 2007; Goodman *et al*., 2008). There is some evidence that improving the efficacy of conventional cleaning/disinfection can reduce the acquisition of pathogens (Dancer *et al*., 2009; Datta *et al*., 2011; Hayden *et al*., 2006). For example, Hayden *et al*. (2006) performed a 9-month prospective before and 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. 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 (Fitzgerald *et al*., 2012). However, compliance soon returned towards 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% (Rutala and Weber, 2011).

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 (Jeanes *et al*., 2005; Manian *et al*., 2011), risking damage (corrosion) to materials (Dettenkofer and Block, 2005; McGowan *et al*., 1988) and presenting health risks for operators (Mirabelli *et al*., 2007), can have limited success in removing environmental reservoirs of pathogens (Byers *et al*., 1998; Manian *et al*., 2011; Morter *et al*., 2011). For example, an average of 2.8 rounds of quaternary ammonium compound disinfections were required to eradicate VRE from a room in one study (Byers *et al*., 1998) and *A. baumannii* or MRSA were cultured from 27% of rooms sampled after four rounds of cleaning and bleach disinfection (Manian *et al*., 2011). NTD systems offer the potential to overcome some of these problems (Byrns and Fuller, 2011; Davies *et al*., 2011; Falagas *et al*., 2011).

17.5 Overview of NTD systems

The most commonly used NTD systems in healthcare are 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 UVC systems (such as Lumalier Tru-D) (Boyce, 2009; Davies *et al*., 2011; Falagas *et al*., 2011; Orlando *et al*., 2008; Rutala and Weber, 2011). A fourth class of NTD system based on PX-UV radiation has been introduced recently and has been the subject of few limited studies so far (Stibich *et al*., 2011).

Considering what would make an 'ideal' NTD system is useful in comparing the features of the various systems available (Table 17.1). The 'ideal' system would have a short cycle time; a high efficacy to eliminate pathogens from surfaces; homogeneous 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.

Table 17.1 An overview of 'no-touch' automated room disinfection systems

The 'ideal' NTD system	Aerosolised hydrogen peroxide (aHP)	H_2O_2 vapour	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	✗	✓	✗	✗
US EPA registered	✗	✓ (Sterilant)	✗	✗
UK Rapid Review Panel recommendation[b]	3	1 (HPV); 2 (VHP)	✗	✗
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.
[b] Rapid review panel recommendations are as follows:

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.
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.
3. A potentially useful new concept but insufficiently validated; more research and development is required before it is ready for evaluation in practice.

17.5.1 Commonly used systems

aHP

aHP systems deliver a pressure-generated aerosol. The systems used most commonly in healthcare use a solution containing 5–6% hydrogen peroxide and <50 ppm silver (Fig. 17.3) (Chan *et al*., 2011; Orlando *et al*., 2008; Otter and Yezli, 2011; Otter *et al*., 2010b; Shapey *et al*., 2008). These systems are sometimes known as 'dry-mist hydrogen peroxide', though this term is a poor reflection of their properties (Andersen *et al*., 2010; Barbut *et al*., 2009). Aerosolised droplets are introduced into an enclosure via a unidirectional nozzle (Boyce, 2009; Rutala and Weber, 2011). One manufacturer (ASP Glosair) states a particle size of 8–10 µm (Fu *et al*., 2012; Holmdahl *et al*., 2011) whereas another (Oxypharm Nocospray) states a smaller particle size of 0.5 µm (Orlando *et al*., 2008). 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 (Andersen *et al*., 2006; Holmdahl *et al*., 2011). Following exposure, the aerosol is usually left to decompose naturally, without any active aeration.

H_2O_2 vapour

H_2O_2 vapour systems deliver a heat-generated vapour of 30–35% w/w aqueous hydrogen peroxide through a high-velocity air stream to achieve homogeneous distribution throughout an enclosed area (enclosure) (Fig. 17.4) (Boyce, 2009; Otter and Yezli, 2011). Two systems using H_2O_2 vapour are available commercially – Bioquell and Steris. Bioquell systems are usually termed hydrogen peroxide vapour (HPV) and Steris systems vaporized hydrogen peroxide (VHP). Bioquell HPV includes a generator to produce HPV, a module 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 (Hall *et al*., 2007; Ray *et al*., 2010). 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 '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 while the Steris systems hold a steady H_2O_2 air concentration throughout the exposure period.

17.3 Aerosolised hydrogen peroxide (aHP) systems: (a) ASP Glosair; (b) Steris Biogienie.

(a)

(b)

17.4 H_2O_2 vapour systems: (a) Bioquell hydrogen peroxide vapour (HPV); (b) Steris vaporized hydrogen peroxide (VHP).

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. 17.5) (Boyce *et al.*, 2011; Nerandzic *et al.*, 2010; Rutala *et al.*, 2010). The device is placed in the centre of the room and commonly 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 (Boyce *et al.*, 2011). 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.

PX-UV

PX-UV systems emit broad spectrum UV in short pulses (Fig. 17.5) (Stibich *et al.*, 2011). They are placed at multiple room locations and have a relatively short cycle time.

17.5 Ultraviolet radiation systems: (a) UVC: Lumalier Tru-D; (b) pulsed xenon UV (PX-UV): Xenex.

17.5.2 Microbiological efficacy

Studies evaluating the *in vitro* and *in situ* efficacy of NTD systems are summarised in Tables 17.2 and 17.3, respectively. One aHP system (ASP Glosair) achieves a ~4-log reduction on *C. difficile* spores *in vitro* (Barbut *et al*., 2009) and has limited capacity to inactivate commercially produced 6-log spore biological indicators (BIs) (Andersen *et al*., 2006; Holmdahl *et al*., 2011). Catalase-positive bacteria are considerably less susceptible to the low concentration of H_2O_2 used by aHP systems than catalase-negative bacteria or metabolically inert spores (Otter and French, 2009; Pottage *et al*., 2012). 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* (Fu *et al*., 2012; Piskin *et al*., 2011) and tuberculocidal activity (Andersen, 2010; Andersen *et al*., 2010; Beswick *et al*., 2011; Grare *et al*., 2008). aHP systems have been shown to reduce contamination of *C. difficile* and MRSA on hospital surfaces (Bartels *et al*., 2008; Barbut *et al*., 2009; Chan *et al*., 2011; Orlando *et al*., 2008; Shapey *et al*., 2008), but have not been shown to eliminate pathogens in clinical practice. For example, one or more positive *C. difficile* cultures were collected from 20% of 15 (Barbut *et al*., 2009) and 50% of 10 (Shapey *et al*., 2008) rooms studied after an aHP process.

Both Bioquell HPV and Steris VHP systems are Environmental Protection Agency (EPA)-registered sterilants, which means they have passed the AOAC sporicide test on porous and non-porous surfaces (Humphreys, 2011). Both systems are associated with the elimination of pathogens from surfaces *in situ* (Bates and Pearse, 2005; Boyce *et al*., 2008; Hardy *et al*., 2007; Jeanes *et al*., 2005; Manian *et al*., 2011; Otter *et al*., 2008, 2010c; Ray *et al*., 2010) and cycles are validated by a >6-log reduction of *Geobacillus stearothermophilus* BI spores (Bates and Pearse, 2005; Boyce *et al*., 2008; Hardy *et al*., 2007; Jeanes *et al*., 2005). HPV and VHP are sporicidal, bactericidal, mycobactericidal and virucidal, achieving a >6-log reduction against a wide range of nosocomial pathogens including *C. difficile* spores, MRSA, VRE, *A. baumannii* and norovirus surrogates (Barbut *et al*., 2012; Bentley *et al*., 2012; Berrie *et al*., 2011; Goyal *et al*., 2011; Hall *et al*., 2007; Otter and French, 2009; Pottage *et al*., 2010), though efficacy may be reduced by high microbial loading and the presence of organic soil (Fu *et al*., 2012; Otter and French, 2009; Otter *et al*., 2012; Pottage *et al*., 2010).

UVC produces a dose-dependent 2 to 4-log reduction of nosocomial pathogens experimentally dried onto surfaces but the microbiological reduction is significantly lower out of direct line of sight of the device (Boyce *et al*., 2011; Nerandzic *et al*., 2010; Rutala *et al*., 2010). For example, in one study, a 1-log reduction was achieved on *C. difficile* spores inoculated on plastic carriers placed 10 feet (3 m) away from the device out of direct

Table 17.2 Studies evaluating the *in vitro* efficacy of 'no-touch' automated room disinfection systems

Author	Year	Setting	Design	Results
H_2O_2 vapour				
Barbut *et al.* (2012)	2012		Plastic or laminate carriers with 5–6 log of *C. difficile* spores exposed to HPV in unfurnished, unoccupied 33–45 m^3 rooms.	*C. difficile* was completely eradicated from the exposed carriers regardless of the *C. difficile* strain or surface used.
Otter *et al.* (2012)	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.* (2012)	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.* (2012)	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.* (2012)	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.

Table 17.2 Continued

Author	Year	Setting	Design	Results
Holmdahl *et al.* (2011)	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.* (2011)	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 titre.
Pottage *et al.* (2012)	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.* (2010)	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.
Otter and French (2009)	2009	A 100 m^3 test room	Five strains of MRSA and three stains of VRE, *Acinetobacter* spp., *K. pneumoniae* and *C. difficile* spores were dried on stainless steel discs at concentrations of 5–7-log cfu/carrier either in 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.* (2007)	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.* (2005)	2005	A 0.4 m^3glovebox enclosure	>6-log of two 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.* (2005)	2005	A 64.5 m^3 laboratory room	$8 \times 10^4 - 2.3 \times 10^6$ of two 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.
Aerosolised hydrogen peroxide (aHP)				
Fu *et al.* (2012)	2012	Two rooms to simulate a patient room (50.1 m^3) and an en-suite bathroom (13.2 m^3)	Tyvek-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.*, (2011)	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 two 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 two tests were inactivted.
Piskin *et al.* (2011)	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.	~4 log reduction achieved for MRSA and *A. baumannii*. aHP was less effective for the bacteria dried in serum and in closed or semi-closed locations (e.g. inside a drawer).

Table 17.2 Continued

Author	Year	Setting	Design	Results
Koburger *et al.* (2011)	2011	37 m^3 test room	Carriers inoculated with 4.3, 5.5, and 6.5-log of *Aspergillus brasiliensis.*	aHP achieved 0.4, 1.3 and 4.3-log reductions respectively at the initial fungal loads of 6.5, 5.5, and 4.3-log.
Andersen *et al.* (2010)	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 days' incubation.
Grare *et al.* (2008)	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.* (2008)	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 three aHP decontamination cycles were run.	All samples were negative after one or three aHP cycles.
Andersen *et al.* (2006)	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. Three 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)				
Havill *et al.* (2012)	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.* (2011)	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.*, 2010)	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 μW/cm^2 (vegetative cycle).	UVC achieved a ~3.5-log reduction on the 26 environmental sites and a 2-log reduction on equipment.
Rutala *et al.* (2010)	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, placedat various room locations and exposed to 36 000 μWs/$cm^2$for *C. difficile* (sporicidal cycle) or 12 000 μWs/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.

Table 17.3 Studies evaluating the *in situ* efficacy of 'no-touch' automated room disinfection systems

Author	Year	Setting	Design	Samples contaminated
HPV				
French *et al.* (2004)	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.* (2005)	2005	A UK hospital surgery ward	Environmental sampling for MRSA was conducted before and after HPV decontamination.	Before decontamination, eight (16.0%) of 50 swabs taken were positive for MRSA. After HPV, none (0%) of the 50 swabs yielded MRSA.
Bates and Pearse (2005)	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.* (2006)	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.* (2007)	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.

Otter *et al.* (2007)	2007	A 500-bed hospital	Standardised 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 one (3.3%) of the 30 sites sampled before and after HPV respectively. GNR were isolated from 3 (10.0%) and none (0%) of the 30 sites sampled before and after HPV, respectively. VRE was isolated from one (6.7%) and none (0%) of the 15 sites sampled before and after HPV, respectively.
Boyce *et al.* (2008)	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.* (2008)	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, 1 (3.4%) of the 29 sites (a composite swab from six bed-rails) yielded MRSA.
Otter *et al.* (2008)	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.* (2010c)	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.
[i]Ray *et al.* (2010)	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.*

Table 17.3 Continued

Author	Year	Setting	Design	Samples contaminated
Manian *et al.* (2011)	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 grew fMRSA or ABC.
Barbut *et al.* (2013)	2012	A burn unit	Environmental sampling of surfaces in individual patient's rooms before and after HPV.	Before decontamination, 6% (6/102) of surface samples grew *Acinetobacter*, 4% (4/102) grew *S. aureus* and 2% (2/102) grew *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, grew *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.
Aerosolised hydrogen peroxide (aHP)				
Shapey *et al.* (2008)	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.* (2008)	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.

Barbut *et al.* (2012)	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*.
Ultraviolet-C radiation (UVC)				
Nerandzic *et al.* (2010)	2010	A 202-bed acute care hospital	Motioned swabs were used to sample four sites for MRSA, VRE and *C. difficile* from rooms of 66 discharged patients before and after a sporocidal UVC treatment (22 000 μW s/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.* (2010)	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 μW s/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.
Pulsed-xenon UV (PX-UV)				
Stibich *et al.* (2011)	2011	A cancer centre	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.

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

line of sight, compared with 2.6-log in direct line of sight (Nerandzic *et al*., 2010). 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; however, there was incomplete inactivation of *C. difficile*, VRE, *Acinetobacter* or MRSA on hospital surfaces (Boyce *et al*., 2011; Nerandzic *et al*., 2010; Rutala *et al*., 2010).

A PX-UV system (Xenex) achieved a significant reduction in VRE contamination in a room in a 12 minute cycle (Stibich *et al*., 2011). Further efficacy data are awaited.

17.5.3 Clinical impact

HPV has been used to remove environmental reservoirs during outbreaks of *C. difficile* (Cooper *et al*., 2011), MRSA and meticillin-susceptible *S. aureus* (MSSA) (Dryden *et al*., 2008; Jeanes *et al*., 2005; Otter *et al*., 2008) multidrug-resistant Gram-negative bacteria (Bates and Pearse, 2005; Kaiser *et al*., 2011; Otter *et al*., 2010c) and other pathogens (Otter *et al*., 2010a). VHP has been used for tackling environmental reservoirs during outbreaks of *A. baumannii* in two reports (Chmielarczyk *et al*., 2012; Ray *et al*., 2010). 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 (Passaretti *et al*., 2013). Thus, HPV decontamination successfully mitigated the risk from the prior room occupant.

Two pre-post studies have evaluated the clinical impact of HPV (Boyce *et al*., 2008; Manian *et al*., 2013). Boyce *et al*. (2008) performed a before and after study showing that HPV decontamination of rooms vacated by patients with *C. difficile* infection (CDI) significantly reduced the 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. Manian *et al*. (2011) performed a before and after study showing that HPV decontamination of rooms vacated by patients with CDI (or quadruple bleach disinfection where HPV was not available) significantly reduced the hospital-wide incidence of CDI by 37%. Whilst it was not possible to differentiate the impact of introducing HPV and quadruple bleach disinfection, a previous study by the same group showed that quadruple bleach disinfection was necessary to eliminate *A. baumannii* and MRSA from surfaces, and that HPV was microbiologically superior to quadruple bleach disinfection. Thus, since HPV has time and efficiency savings

compared with quadruple bleach disinfection, it was cost effective to use HPV in this setting (Manian *et al.*, 2013).

Currently, there is no published evidence that disinfection with aHP, UVC or PX-UV systems reduce epidemic or endemic infection rates.

17.5.4 Practical considerations

aHP systems

aHP is straightforward to use 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 (Holmdahl *et al.*, 2011). 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 (Fu *et al.*, 2012). Reported cycle times are 3–4 hours for multiple cycles (Bartels *et al.*, 2008; Holmdahl *et al.*, 2011) and 2 hours for single cycles (Shapey *et al.*, 2008). 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 (Fu *et al.*, 2012). Several studies suggest that homogeneous distribution of the active agent is not achieved (Fu *et al.*, 2012; Holmdahl *et al.*, 2011; Shapey *et al.*, 2008), perhaps because aHP is introduced via a unidirectional nozzle and the particles are affected by gravity. Sub-lethal exposure to hydrogen peroxide or silver could result in the development of tolerance or resistance (Chopra, 2007; McDonnell and Russell, 1999; Meyer and Cookson, 2010). The potential for transferable resistance to silver is greater than for hydrogen peroxide due to plasmid-mediated silver resistance genes (Chopra, 2007; McDonnell and Russell, 1999). Data are required confirming the compatibility of aHP systems with common hospital materials, including sensitive electronics. Finally, several studies have noted equipment reliability problems (Beswick *et al.*, 2011; Fu *et al.*, 2012; Shapey *et al.*, 2008), which was a feature of older foggers (Munster and Ostrander, 1974).

H_2O_2 vapour systems

H_2O_2 vapour systems have been used to decontaminate rooms (Boyce *et al.*, 2008; French *et al.*, 2004), multi-bedded bays (Bates and Pearse, 2005, Boyce *et al.*, 2008; Dryden *et al.*, 2008) and entire units (Boyce *et al.*, 2008; Jeanes *et al.*, 2005; Otter *et al.*, 2010c). However, H_2O_2 vapour 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 H_2O_2 inside the enclosure is below health and safety exposure limits (1 ppm) before re-entry. Thus, staff training requirements for using H_2O_2 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 ensures that few microorganisms undergo sub-lethal exposure. Reported cycle times are currently 1.5–2.5 hours for a single room for HPV (Department of Health, 2009; Otter and Yezli, 2010) and 8 hours for VHP (Ray *et al.*, 2010). The compatibility of HPV with hospital materials, including sensitive electronics, is well established (EPA, 2010a). A recent study reported incompatibility of HPV with one brand of paint that was rectified by replacing the paint with a different brand (Passaretti *et al.*, 2013).

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 46–86 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 (Boyce *et al.*, 2011). 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 (Memarzadeh *et al.*, 2010; Reeda, 2010). 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 (Harrington and Valigosky, 2007). The long-term impact of UVC on hospital materials has not been described (Tyan *et al.*, 2002). UVC is relatively expensive compared with other NTD systems (ECRI, 2011). Finally, UV radiation is a known mutagen (Anderson, 1995); since UVC systems do not inactivate all microbes in the room, a proportion of those that have received a sub-lethal 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. However, given the short cycles associated with PX-UV, it should be prioritised for further evaluation.

17.5.5 Other systems

Gaseous ozone for room disinfection has also been evaluated (Moat *et al.*, 2009; Sharma and Hudson, 2008). 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 (Moat *et al.*, 2009) but a >4-log spore reduction in the other (Sharma and Hudson, 2008). Both evaluations tested the systems at high humidity, one at 80–90% (Moat *et al.*, 2009) and one at >95% (Sharma and Hudson, 2008). Another system used a high concentration of gaseous ozone (80 ppm) and up to 3% aHP combined with high humidity (80%) to achieve a >6-log reduction of various hospital pathogens *in vitro* (Zoutman *et al.*, 2011). Substantially lower reductions were achieved at lower relative humidity (Zoutman *et al.*, 2011). The requirement for high humidity is a major practical limitation for ozone-based systems (Li and Wang, 2003). 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 measurements to assure that the room is safe to enter are necessary for these systems in the healthcare setting (OSHA, 2005). Data on the compatibility of this process with hospital materials are needed, given ozone's known corrosive properties (Davies *et al.*, 2011).

Chlorine dioxide has a high level of efficacy against a range of pathogens (Beswick *et al.*, 2011). However, concerns about safety and material compatibility mean that it is unlikely to be used in healthcare settings (Beswick *et al.*, 2011, EPA, 2010a).

'Fogging' with various chemicals, including super-oxidised water (Clark *et al.*, 2006; Galvin *et al.*, 2012), solutions of H_2O_2 (Taneja *et al.*, 2011; Tuladhar *et al.*, 2012) and other chemicals (Callahan *et al.*, 2010; De Lorenzi *et al.*, 2011; Friedman *et al.*, 1968; Ostrander and Griffith, 1964), have been evaluated. 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 (Taneja *et al.*, 2011), with associated risks to operators. Data on compatibility with hospital materials are awaited.

17.5.6 Comparing 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 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 NTD systems produce a more significant reduction of bacterial contamination than conventional disinfection (Barbut *et al*., 2009; Boyce *et al*., 2011; French *et al*., 2004; Manian *et al*., 2011; Nerandzic *et al*., 2010; Shapey *et al*., 2008). However, comparison of the relative effectiveness of different NTD systems is difficult because of variations in sample sites (especially orientation and proximity to the NTD device), patient infection or colonisation status, the organism, the microbiological testing methods and the type of pre-cleaning. Thus, the best way to compare different systems is through controlled head-to-head studies (Boyce, 2009), ideally using outcomes related to reduced transmission in clinical settings. However, there have been few studies comparing these outcomes, so it is not possible to evaluate the relative clinical impact of NTD systems using current data. Thus, the available head-to-head studies are currently the most useful way to compare NTD systems.

A recently published study comparing HPV (Bioquell) with an aHP system (ASP Glosair) was performed by St George's Hospital, London (Fu *et al*., 2012). 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 H_2O_2 are 1 ppm as an 8-hour time weighted average, or 2 ppm for 15 minutes as a short-term exposure limit (STEL) (Health and Safety Executive, 2005). The HPV manufacturer mandates re-entering the room only after the measurable concentration of H_2O_2 is <1 ppm; the aHP manufacturer recommended room re-entry 2 hours after the start of the cycle. Thus, in this study the mean concentration of H_2O_2 in the room was measured 2 hours after the cycle started for both systems. The mean H_2O_2 concentration in the room 2 hours 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 H_2O_2 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. More than 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 H_2O_2 systems.

Microbiological efficacy was assessed by using commercially available 6-log *G. stearothermophilus* BIs and in-house prepared test discs inoculated with MRSA, *A. baumannii* and *C. difficile* (spores) placed at 11 locations around the room (Fu *et al*., 2012). In addition, in-house prepared test discs dried in 3% or 10% bovine serum albumin (BSA) to simulate dirty conditions were tested in two further room locations. There are no standard testing methods for NTD 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 3% 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 sub-optimal pre-cleaning. 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 Malmö, 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 (Holmdahl *et al*., 2011). 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 (Fu *et al*., 2012).

The UK Health and Safety Laboratory performed a detailed head-to-head study of six room decontamination technologies including HPV and aHP systems (Beswick *et al*., 2011). 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 (Beswick *et al*., 2011; Fu *et al*., 2012; Holmdahl *et al*., 2011). 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) (Havill *et al*., 2012). In-house prepared carrier discs inoculated with ~10^6 *C. difficile* spores and BIs with 10^4 and 10^6 *G. stearothermophilus* spores were placed in five sites (three 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.

No head-to-head studies comparing aHP and UVC have been published. More head-to-head evaluations of all NTD systems are required, including assessment of clinically relavent outcomes.

17.5.7 Cost

NTD 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 (Department of Health, 2009).

Several factors must be taken into account when considering the cost of NTD systems. For hospitals that purchase their own 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 and 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 NTD 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$3 000) per month over a 36 month lease (ECRI, 2011). Thus, the relative purchase cost of equipment is likely to be UVC > PX-UV > H_2O_2 vapour systems > aHP (ECRI, 2011). 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 NTD systems have been published. Performing a cost-effectiveness study on the use of an NTD 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 (Perencevich *et al.*, 2007).

17.6 When to consider an NTD system

Current CDC guidelines recommend against routine 'disinfectant fogging' in patient-care areas (Rutala *et al.*, 2008). This recommendation is currently being re-evaluated by the CDC based on data that have emerged since the guidelines were published and suggest NTD systems may be warranted in some circumstances. The strongest reason for considering an NTD system is to break the chain of transmission by improving terminal disinfection of clinical areas after patients infected or colonised with certain pathogens have been discharged (Otter *et al.*, 2011; Rutala and Weber, 2011). Key pathogens associated with contamination of the environment include *C. difficile*, VRE, MRSA, *A. baumannii, P. aeruginosa* and norovirus (Otter *et al.*, 2011).

Because of practicality, cost and resource constraints, NTD 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 colonised with multiple MDROs (Otter *et al.*, 2007). 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 intensive care unit (ICU) (Hardy *et al.*, 2007). NTD systems have been used to control endemic infection (Boyce *et al.*, 2008; Otter *et al.*, 2011; Rutala and Weber, 2011) and outbreaks (Bates and Pearse, 2005; Cooper *et al.*, 2011; Dryden *et al.*, 2008; Jeanes *et al.*, 2005; Kaiser *et al.*, 2011; Otter *et al.*, 2010c; Ray *et al.*, 2010). Whilst disinfection of single rooms is more common, NTD systems have

been used to disinfect multi-occupancy areas, particularly to remove environmental reservoirs during outbreaks (Bates and Pearse, 2005; Boyce *et al*., 2008; Dryden *et al*., 2008; Jeanes *et al*., 2005; Otter *et al*., 2010c) and whole wards have been disinfected in some studies (Boyce *et al*., 2008, Jeanes *et al*., 2005, Otter *et al*., 2010c). The different indications for the use of NTD systems are outlined in the following scenarios.

17.6.1 Scenarios when the use of an NTD system may be indicated

The choice of whether to rely on current cleaning and disinfection methods, enhanced conventional methods or an NTD system will be determined by the clinical scenario. The key factors are whether the area to be disinfected is a single room or a multi-occupancy 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 (Barbut *et al*., 2009; Boyce *et al*., 2008; Otter *et al*., 2010c; Passaretti *et al*., 2013; Shapey *et al*., 2008). 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 colonisation 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, paediatric or adult intensive care.

The disinfection of multi-occupancy bays using NTD systems is constrained by the need to accommodate patients elsewhere during the disinfection process (Otter *et al*., 2009b). 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 (Nerandzic *et al*., 2010; Rutala *et al*., 2010) but practical constraints limit the use of hydrogen peroxide NTD systems in this situation. Conversely, H_2O_2 vapour 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 (Boyce *et al*., 2008; Manian *et al*., 2011; Otter *et al*., 2010a). 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 (Bartels *et al*., 2008; Boyce *et al*., 2008; French *et al*., 2004; Nerandzic *et al*., 2010; Shapey *et al*., 2008). Enhanced conventional disinfection methods should also be employed in these scenarios (Dancer *et al*., 2009; Datta *et al*., 2011; Hayden *et al*., 2006; Mahamat *et al*., 2007; Mayfield *et al*., 2000; Wilcox *et al*., 2003), 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 (Datta *et al*., 2011; Manian *et al*., 2011; Morter *et al*., 2011; Wilcox *et al*., 2003).

Other potential applications of NTD systems include: the removal of environmental pathogens disturbed during building works such as *Aspergillus fumigatus* (Vonberg and Gastmeier, 2006); as part of emergency preparedness planning (Otter *et al*., 2010a); the disinfection of mobile medical equipment in a dedicated facility; and decontamination of emergency vehicles or operating theatres (van't Veen *et al*., 2005). 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 (Boyce *et al*., 1997; Dryden *et al*., 2008; Dumford *et al*., 2009) means that dedicated disinfection rooms incorporating NTD systems are becoming recognised as very useful hospital facilities.

17.7 Using, validating and regulating NTD systems

17.7.1 The need for pre-cleaning

As with all forms of decontamination, cleaning is required prior to NTD disinfection system use in order to remove organic matter that reduces the effectiveness of NTD systems (Fu *et al*., 2012; Kac *et al*., 2010; Otter and French, 2009; Otter *et al*., 2012; Pottage *et al*., 2010; Sweeney and Dancer, 2009). 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 (Otter *et al*., 2012). The effectiveness of HPV was reduced as the concentration of BSA increased. There is evidence that some NTD 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 (Fu *et al*., 2012).

Nevertheless, several studies demonstrate that NTD systems can produce significant reductions in environmental contamination even without pre-cleaning (French *et al*., 2004; Nerandzic *et al*., 2010; Rutala *et al*., 2010). For example, in one study, 1 site out of 85 sampled yielded MRSA after HPV without pre-cleaning compared with 61 (72%) of 85 matched sites before

HPV (French *et al*., 2004). 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.

17.7.2 Validation

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

NTD systems could be validated by routine microbiological sampling using conventional standards (Dancer, 2004), but this 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 (Boyce *et al*., 2008; Holmdahl *et al*., 2011). The question remains as to whether 6-log BIs are an appropriate test for validating NTD systems, given that the concentration of contamination on hospital surfaces is usually in the 2-log range (Holmdahl *et al*., 2011; Otter and Yezli, 2012; Walder and Holmdahl, 2012). Walder and Holmdahl (2012) argue that soiling and biofilms (Smith and Hunter, 2008; Vickery *et al*., 2012), occasional higher levels of contamination (Morter *et al*., 2011), the occurrence of pathogens with reduced susceptibility to certain agents (Pottage *et al*., 2012) and the potential for incomplete distribution (Fu *et al*., 2012; Havill *et al*., 2012; Holmdahl *et al*., 2011) mean that 6-log BIs are an appropriate target for NTD systems. Recent evidence published by Pottage *et al*. (2012) and others (Beswick *et al*., 2011; Fu *et al*., 2012; Otter and French, 2009) indicating that catalase-positive bacteria are less susceptible to hydrogen peroxide-based NTD systems than bacterial endospores provides a further reason to use stringent challenges for these systems (Otter and Yezli, 2012).

The US EPA requires a hospital disinfectant to achieve a >6-log reduction of certain vegetative bacteria *in vitro* (EPA, 2010b). 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 NTD systems when the elimination of pathogens is required (Otter and Yezli, 2012; Walder and Holmdahl, 2012). H_2O_2 vapour systems can eliminate pathogens from surfaces, produce a >6-log reduction of a range of pathogens *in vitro* and can inactivate 6-log BIs (Boyce *et al*., 2008; French *et al*., 2004; Otter and French, 2009; Otter *et al*., 2010c). aHP, UVC and PX-UV are much less effective in these tests (Andersen *et al*., 2006; Barbut *et al*., 2009;

Boyce *et al*., 2011; Fu *et al*., 2012; Holmdahl *et al*., 2011; Nerandzic *et al*., 2010; Rutala *et al*., 2010; Shapey *et al*., 2008). However, further studies are necessary to determine the level of pathogen reduction required to interrupt transmission and set the appropriate clinical decontamination standard for NTD systems.

17.7.3 Regulation

Given the relatively recent introduction of NTD 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) (Low, 2011). Testing standards are generally not specified for NTD systems, although a French standard for testing NTD systems, NF72-281, is currently under evaluation for adoption as a European standard. Currently, it is not clear how the BPD will influence NTD systems, although the NTDs will need to be assessed and registered as with any other disinfectant.

In the UK, the Health and Safety Executive, Department of Health (DH), Health Protection Agency (HPA) and various professional societies have a role to play in the regulation of NTD systems. In England, the DH and HPA have established a expert group called the Rapid Review Panel (RRP) to evaluate products claiming to be useful in healthcare applications (Department of Health, 2009). The RRP has issued several recommendations on NTD systems. These provide independent, evidence-based recommendations that can guide decision making about such products. The RRP has issued the following recommendations about NTD systems (which 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 US, the EPA regulates disinfectant use and will likely regulate NTD systems. The EPA issued an order to stop a US hospital using a disinfectant fogger in ambulances on safety grounds (EPA, 2011). 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) (SHEA/APIC/AHA, 2011) illustrates that healthcare regulators and professional societies are beginning to take an interest in NTD systems. Similarly, ANSM (previously AFSSAPS), the French regulatory body, has withdrawn several NTD systems, including an aHP system, from the French market due to a lack of efficacy data (AFSSAPS, 2011).

Regulators and professional societies will be required to make recommendations on issues such as nomenclature of NTD 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 (Otter and Yezli, 2011; Otter *et al*., 2010b) as using 'hydrogen peroxide vapour' (Chan *et al*., 2011) and correctly as using an aerosol of hydrogen peroxide (Orlando *et al*., 2008). Such confusion in describing the various different NTD systems is also evident in several review papers (Davies *et al*., 2011, Falagas *et al*., 2011).

17.8 Sources of further information and advice

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 NTD systems are potentially an effective and efficient adjunct to decontaminating complex environmental surfaces. As the evidence base grows, the indications and cost-effectiveness of NTD systems will become clearer. At present, there is good evidence that terminal disinfection of clinical areas used by patients colonised 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 NTD 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 decisions.

Technological developments mean that existing NTD systems will become more refined. For example, improvement in aeration capacity has reduced HPV process times from >4 hours (French *et al*., 2004) to <2 hours for a single room (Barbut *et al*., 2012; Otter and Yezli, 2010). Also, the use of UV reflective paint could reduce the impact of line-of-sight issues for UV systems (Rutala, 2012). In addition, there seems to be a natural synergy between the use of NTD systems and antimicrobial surfaces or air disinfection systems, which can help to reduce the extent of surface contamination during the stay of a patient (Sexton *et al*., 2006; Weber and Rutala, 2012). The emergence of novel NTD systems, combining rapid cycle times with high-level efficacy, would broaden the potential application of NTD systems.

17.9 Conclusion

There is now evidence that existing 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. Further evidence on the optimal application and cost effectiveness of NTD systems in healthcare is required, but NTD systems are already beginning to be integrated into hospital disinfection policies (Boyce *et al*., 2008; Passaretti *et al*., 2013). Regulators and professional bodies should decide on the terminology and insist on standardisation 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 NTD systems in healthcare settings (Department of Health and Health Protection Agency, 2009; Rutala *et al*., 2008).

Current data on NTD systems in the academic literature is limited but increasing (Fig. 17.1). Academic reviews of NTD systems can provide useful background data, for example, those by Otter *et al*. (2013), Davies *et al*. (2011) and Falagas *et al*. (2011). In addition, publications in the non-peer reviewed literature and by research institutes can provide useful background information. For example, the ECRI Institute (2011) and *Infection Control Today* (Pyrek, 2011) have published useful guidance documents. In addition, several studies of NTD systems with clinical outcomes are currently in progress, including a CDC-funded assessment of a UVC system.[b] These studies will be important in determining the appropriate use of the various

[b] http://www.dukehealth.org/health_library/news/duke-receives-part-of-10-million-grant-from-cdc-to-help-reduce-health-care-associated-infections.

NTD systems. Finally, NTD systems are increasingly included in certain guidelines as an adjunct to traditional cleaning and disinfection (APIC, 2010; Department of Health and Health Protection Agency, 2009).

17.10 References

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