EDITORIAL COMMENTARY

Climbing the Evidentiary Hierarchy for Environmental Infection Control

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(See the Major Article by Passaretti et al, on pages 27–35.)

Increasing concern over multidrug-resistant organisms (MDROs), especially vancomycin-resistant enterococci (VRE), *Clostridium difficile*, and multidrug-resistant gram-negative bacteria (MDR-GNB), has led to increasing attention being paid to the role of high-touch environmental surfaces in transmission. Our current understanding of the roles of environmental surfaces in MDRO transmission include the following: (1) a primary role with transmission from source patient to environmental surface to subsequent patient, and (2) a secondary role from source patient to environmental surface to hands of healthcare personnel to subsequent patient. Either a prior room occupant or a contemporaneous patient sharing reusable medical equipment is the source patient in most primary transmission events.

Standard environmental cleaning and disinfection entails manual cleaning and application of a disinfectant, often utilizing a detergent disinfectant. In addition to new disinfectants with greater potency and shorter contact times, new technological advances include "non-touch disinfection" (NTD) methods, the most developed of which are hydrogen peroxide vapor (HPV), and automated germicidal ultraviolet irradiation. Both methods appear highly efficacious in inactivating the microbial bioburden present on surfaces, and both remove much of the variance inherent in human cleaning activity via a high degree of automation and feedback loops for verification that contact or irradiation times are adequate [1–3].

Despite these advances, demonstrating the clinical impact of both old and new environmental cleaning and disinfection technologies remains challenging. We propose an evidentiary hierarchy for assessing any environmental disinfection strategy (Figure 1), beginning with a foundation (ie, level I) of laboratory efficacy studies similar to those required for registration by the Environmental Protection Agency [4]. Numerous patient and practice factors confound the relationship between environmental bioburden reductions and MDRO transmission interruption, from the number of patients on antibiotics with wounds, devices, and diarrhea (rendering them either more contagious or susceptible to colonization), to rates of compliance with hand hygiene and isolation, to interventions aimed at source control such as chlorhexidine bathing. Because only a small proportion of all MDRO acquisitions lead to eventual infection, linking infection reductions to environmental bioburden reductions (ie, level V of Figure 1) is even more challenging. However, because infections correlate more closely than colonization with mortality, excess length of stay, and cost, such linkage will eventually become necessary to calculate the cost-effectiveness of new technologies.

Such a hierarchy can assist the development of a new disinfection technology, guiding industry in demonstrating achievement at a lower level in the hierarchy before investment is made at a higher level. It also highlights the need for tools to link achievements at lower levels (eg, achievable $\log_{10}$ reductions in the laboratory or as part of an in-use study) to the likelihood of success at a higher level. Standardized methods for environmental and hand sampling, microbiologic cultures, and assessment of adherence to standard environmental cleaning, hand hygiene, and isolation precautions will all be important to make the climbing of this hierarchy more efficient.

The report by Passaretti et al in this issue of *Clinical Infectious Diseases*, in which investigators found that HPV decontamination of MDRO patient rooms was associated with a 45% reduction in environmental contamination and 80% reduction in acquisition of VRE among patients with a prior MDRO-colonized

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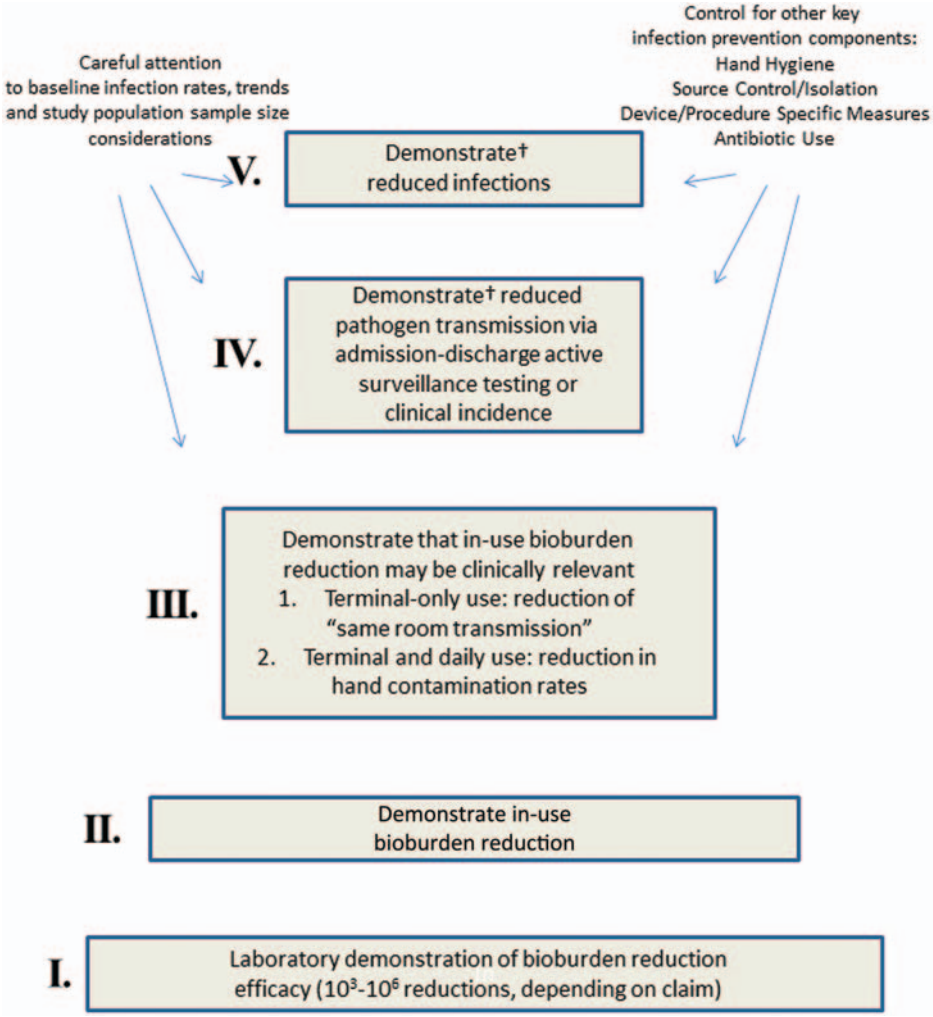

Figure 1. Evidence hierarchy for increasing patient safety through healthcare environmental surface cleaning and disinfection.†Prioritize cluster randomization over interrupted time series design.

room occupant, fits in the middle of this proposed hierarchy (ie, level III of Figure 1) [5]. The focus on possible transmission from a prior room occupant follows from HPV decontamination being practical only for terminal and not daily room cleaning and disinfection. In another recent study using performance-improved standard cleaning and disinfection methods, methicillin-resistant *Staphylococcus aureus* (MRSA) acquisition was reduced by 62% and VRE by 22% in patients with a prior room occupant colonized by the respective MDRO [6].

In previous studies, 19% of all MRSA, 18%–38% of VRE, and 11% of *C. difficile* acquisitions or infections occurred in patients where the prior room occupants were known to be colonized or infected by the respective MDRO [7–9]. By extrapolating the unadjusted data in Table 2 of the report by Passaretti et al, it appears that, had HPV decontamination not been used, approximately 25% of all VRE, 23% of MRSA, 29% of all MDR-GNB, and 28% of *C. difficile* acquisitions or infections would have occurred in patients with a prior room occupant colonized or infected with ≥1, but not necessarily respective, MDROs [5]. However, only a fraction of these MDRO acquisitions are the result of primary environmental transmission. Huang et al estimated that the excess risk for acquisition from a colonized or infected prior room occupant represented only 5.1% of the overall risk for MRSA acquisition and 6.8% of the risk for VRE [7]. Other data show that, despite being highly efficacious in reducing bioburden, recontamination occurs quickly following HPV room decontamination [1]. If NTD or other new technologies feasible only for terminal decontamination are going

to climb to higher evidentiary levels and demonstrate impact on overall MDRO transmission (ie, level IV of Figure 1) they will probably need to be coupled with more reliable methods of daily cleaning and disinfection.

Intervention and control wards in the study by Passaretti et al were located all in a single hospital and it is unclear whether the assignment of the intervention to certain units was random [5].

Moreover, there was mixing across time periods, with transmission opportunities on all the wards during the preintervention phase, along with the opportunities on the control wards during the intervention phase, serving as collective controls to the opportunities on the HPV wards during the intervention phase. While this design was adopted to increase the size of the study, secular trends in rates across all units could result in a significant association with the intervention introduced late in the overall study period. However, the modeling performed by these investigators controlled for rates and time and still found a significant association with HPV decontamination.

Although there was a mortality risk index included in Passaretti et al's model, there was no direct measure of factors such as invasive devices, antibiotic exposures, presence of wounds, or diarrhea. In addition, there was no reported measure of institutional factors such as compliance with hand hygiene or isolation precautions. It is possible, though not probable, that because HPV decontamination involves use of sophisticated equipment and processes, there was greater awareness by healthcare personnel of the importance of infection control, leading to higher levels of compliance with hand hygiene and isolation precautions.

Finally, there was no report on the adequacy of standard cleaning and disinfection, and the method used to assess adequacy—direct observation by study personnel—is severely limited by the Hawthorne effect. This is probably one of the greatest limitations of this study; while it demonstrates superiority of HPV decontamination in preventing a minor subset of transmission events, the reader is left with the question "compared to what?" Future studies should include measures of the adequacy of cleaning and disinfection in a control based on more standardized, reliable methods [10].

Other data helpful in understanding these findings would have been full characterization (ie, strain type) of both patient and environmental MDRO isolates, including those from prior and subsequent room occupants when transmission was assumed to have occurred. Importantly, discordant MDRO transmission events (ie, prior occupant with 1 MDRO, subsequent occupant found with another MDRO species) were included in this study to assess clinical effectiveness of HPV room decontamination. The frequent finding of MDRO environmental contaminants that differed from the recent room occupant would appear to support this inclusion.

Surprisingly, 13.9% of rooms were still contaminated after HPV decontamination (ie, Table 5 in the report by Passaretti et al), despite the remarkable efficacy of HPV decontamination [1, 2]. Although the culture methods used may have been overly sensitive (ie, broth amplifying as little as 1 colony-forming unit), this may have been offset by a relatively small, and therefore relatively insensitive, surface area sampled (25 cm^2). Because environmental contamination has a probabilistic relationship to transmission, the sampling of larger surface areas using quantitative culture methods will allow better correlation of in-practice bioburden reductions to the interruption of transmission [11].

Despite these limitations, this is an important study that further elucidates the role of environmental surfaces in transmission. Not only is this the first controlled study showing the potential advantage of an NTD intervention, its focus on "prior-to-subsequent room occupant" transmission was well planned and implemented to achieve sufficient power. Though limited, the environmental culture results show directionality in support of transmission reductions. The investigators are to be commended for their seminal work that will serve as an important guide for future studies.

Notes

Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors: No reported conflicts.

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MAJOR ARTICLE

An Evaluation of Environmental Decontamination With Hydrogen Peroxide Vapor for Reducing the Risk of Patient Acquisition of Multidrug-Resistant Organisms

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Background. Admission to a room previously occupied by a patient with certain multidrug-resistant organisms (MDROs) increases the risk of acquisition. Traditional cleaning strategies do not remove all environmental MDROs. We evaluated the environmental and clinical impact of hydrogen peroxide vapor (HPV) room disinfection.

Methods. We performed a 30-month prospective cohort intervention study on 6 high-risk units in a 994-bed tertiary care hospital. Following a 12-month preintervention phase, HPV was implemented on 3 units to decontaminate the rooms of patients known to be infected or colonized with epidemiologically important MDROs, following their discharge. Monthly environmental samples for MDROs were collected on all study units for 3 preintervention and 6 intervention months. The risk of MDRO acquisition in patients admitted to rooms decontaminated using HPV was compared with rooms disinfected using standard methods.

Results. The prior room occupant was known to be infected or colonized with an MDRO in 22% of 6350 admissions. Patients admitted to rooms decontaminated using HPV were 64% less likely to acquire any MDRO (incidence rate ratio [IRR], 0.36; 95% confidence interval [CI], .19–.70; $P < .001$) and 80% less likely to acquire VRE (IRR, 0.20; 95% CI, .08–.52; $P < .001$) after adjusting for other factors. The risk of acquiring *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus*, and multidrug-resistant gram-negative rods individually was reduced, but not significantly. The proportion of rooms environmentally contaminated with MDROs was reduced significantly on the HPV units (relative risk, 0.65, $P = .03$), but not on non-HPV units.

Conclusions. HPV decontamination reduced environmental contamination and the risk of acquiring MDROs compared with standard cleaning protocols.

Keywords. hydrogen peroxide vapor; environmental contamination; disinfection; decontamination; multidrug-resistant organisms.

Patients shed epidemiologically important pathogens including vancomycin-resistant enterococci (VRE), *Clostridium difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA), and *Acinetobacter baumannii* into their surrounding environment. These organisms remain viable on inanimate objects for days

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to months, and can be transferred from the environment to healthcare workers' hands, providing a mode of transmission to other patients [1–3]. Contamination of hospital rooms and equipment can persist despite cleaning and disinfection [1, 4, 5]. Consequently, admission to a room previously occupied by a patient known to be colonized or infected with VRE, *C. difficile*, MRSA, and/or *A. baumannii* increases the chances of acquiring these pathogens [1, 6–10].

In light of these findings, terminal disinfection following patient discharge should be improved [11]. Educational campaigns, including the use of fluorescent or other markers, improve compliance with cleaning regimens and reduce environmental contamination, and there is evidence this reduces the acquisition of select pathogens [12–15]. However, even aggressive cleaning protocols may not be sufficient to remove contamination with some pathogens [13, 16] and the impact of educational campaigns is difficult to sustain [5, 11–14, 16]. Another approach is the use of automated room disinfection systems including those based on hydrogen peroxide or ultraviolet radiation. Automated systems do not rely on the operator to ensure all surfaces are disinfected and adequate contact time is achieved [11]. However, automated methods must be applied in addition to standard cleaning, require areas to be temporarily vacated of patients and staff (potentially leading to delays in bed availability), and incur additional expense.

Hydrogen peroxide vapor (HPV) decontamination is a sporicidal vapor-phase method that inactivates a range of hospital pathogens in vitro [17] and in situ including surfaces that are difficult to clean (eg, keyboards) [4, 18–20]. HPV is used to eliminate environmental reservoirs contributing to multidrug-resistant organism (MDRO) outbreaks [21–23], and regular use of HPV to decontaminate rooms of patients with MDROs has significantly reduced the incidence of *C. difficile* infection and VRE in some settings [19, 24]. However, these investigations were observational and subject to confounding factors, such as impact of other infection control interventions and lack of intervention control group [25, 26]. Hence, we specifically evaluated the impact of adjunctive use of HPV following standard cleaning on patient acquisition of MDROs in rooms treated with HPV vs those where HPV was not used.

MATERIALS AND METHODS

Setting

The Johns Hopkins Hospital is a 994-bed tertiary referral center. We collected data for 12 months prior to the intervention (January 2007 through December 2007) and subsequently for an 18-month intervention (January 2008 through June 2009). Six high-risk units were included. HPV decontamination (Bioquell, Horsham, Pennsylvania) was performed after routine cleaning and disinfection when possible in 2 single-occupancy intensive care units (ICUs; 19-bed surgical and 22-bed neurosurgical) and a high-risk 30-bed surgical unit (73% single occupancy, 27% double occupancy) during the intervention phase. Standard cleaning and disinfection processes continued on the other 3 "standard cleaning" units (16-bed medical, 18-bed cardiothoracic surgery, and 20-bed surgical oncology ICUs) throughout all study periods. No other cleaning interventions occurred during the study. Of note, 2 of the "standard cleaning" units were also being studied for the impact of daily chlorhexidine bathing during part of the study [27]. All patients admitted to these units during the chlorhexidine interventions were excluded from the analysis.

Policies and Practices

MDRO Surveillance/Isolation

On all study units, nurses collect perirectal swabs for VRE and nasal swabs for MRSA on admission and weekly in patients not known to be colonized. Rectal surveillance cultures were plated directly on Bile Esculin Azide agar with 6 mg/mL vancomycin (BD Diagnostics, Sparks, Maryland) for detection of VRE as described previously [28]. Anterior nares surveillance swabs were plated directly on MRSASelect agar (Bio-Rad Laboratories, Hercules, California) and MRSA was confirmed using standard methods. Compliance with surveillance was monitored, and varied among units. No screening was performed for multidrug-resistant gram-negative rods (MDR-GNR, defined as any gram-negative rod susceptible to no more than 1 class of antimicrobial agents tested). *Clostridium difficile* testing is only performed when clinically indicated using previously described methods [29]. When patients are identified as colonized or infected with MRSA, VRE, *C. difficile*, and MDR-GNR, they are placed on contact precautions. Patients known to be colonized with MRSA or VRE are flagged in the medical record.

Standard Cleaning Practices

Floors and surfaces are cleaned/disinfected daily and after discharge using a quaternary ammonium compound (QAC; 3M, St Paul, Minnesota). The QAC is applied using WetTask wipes (Kimberly-Clark, Roswell, Georgia) for surfaces, where the cleaner/disinfectant is poured into the WetTask bucket to impregnate disposable wipes, and a mop and bucket for floors. A hydrogen peroxide–containing liquid cleaner/disinfectant (Oxivir, Johnson Diversity, Sturtevant, Wisconsin) is used to clean the rooms of patients with *C. difficile*. Study personnel periodically monitored compliance with cleaning and disinfection policies by observing housekeepers.

Environmental Sampling

Monthly sampling was performed in all study units over the last 3 months of the preintervention phase and the first 6

months of the intervention phase. Premoistened swabs (BBL CultureSwab with Liquid Stuart, BD Diagnostics) were used to sample standard environmental surfaces and equipment for MRSA, VRE, and MDR-GNR. Cultured sites on each unit included 1 composite swab from 25-cm^2 areas of the bedrail, computer keyboard, and electronic monitoring equipment in each patient room and separate samples from 3 communal surfaces (telephone, computer keyboard, and keypad of a drug administration station). Following swab collection, premoistened cellulose sponges (Solar Biologicals, Ogdensburg, New York) were used to culture the same surfaces for *C. difficile* and processed in our laboratory using previously described methods [19]. All swabs were incubated overnight in brain-heart infusion broth and then plated onto selective media for MRSA, VRE, and MDR-GNR, then cultured and identified using standard microbiologic methods. After each set of cultures, results were fed back to unit staff.

Definition of Acquisition

Patient data relating to MDROs were obtained through analysis of electronic patient records (Theradoc, Salt Lake City, Utah). All patients without a history of a given MDRO in our records and with a room stay of >48 hours were considered at risk for acquisition of that MDRO and included in the

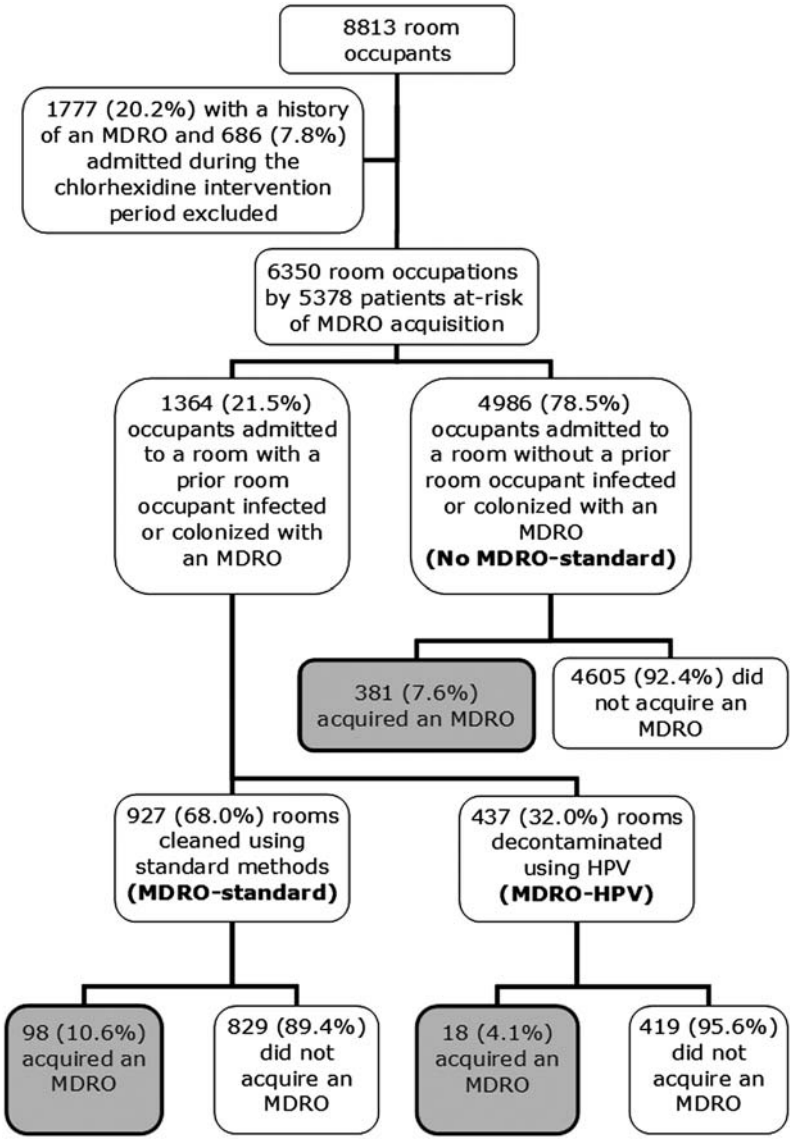

Figure 1. Flowchart of the patient cohort admitted to any study unit by exposure and intervention. Abbreviations: HPV, hydrogen peroxide vapor; MDRO, multidrug-resistant organism.

analysis. Acquisitions were defined as identification of an MDRO after ≥48 hours of admission in a patient with no known prior history of that organism. Each patient admitted to any of the 6 evaluation units during the study period was assigned to one of 3 cohorts, regardless of study unit or phase: (1) MDRO-standard, for patients admitted to a room where the prior room occupant had an MDRO and the room was cleaned and disinfected using standard methods; (2) MDRO-HPV, for patients admitted to a room where the prior room occupant had an MDRO and the room was cleaned and disinfected using standard methods followed by HPV decontamination; and (3) No MDRO-standard, for patients admitted to a room where the prior room occupant was not known to have an MDRO and the room was cleaned and disinfected using standard methods (see Figure 1).

HPV Decontamination

The surgical ICU was vacated and the entire unit, including common areas, decontaminated using HPV at the start of the intervention. Each room on the other 2 HPV units was decontaminated individually using HPV as patients were discharged at the start of the intervention. During the intervention, when possible, the rooms of patients known to be colonized or infected with MDROs were decontaminated using HPV after patient discharge and before the next admission on the 3 HPV units. Equipment from other patient rooms and equipment shared by multiple patients was commonly placed in rooms during decontamination. HPV decontamination was conducted by dedicated personnel as described previously [19] following standard cleaning/disinfection. HPV decontamination required approximately 1.5–3 hours. Each cycle was validated using one 6-log *Geobacillus stearothermophilus* biological indicator (Apex Laboratories, Sanford, North Carolina) that were placed in the corner of the room and cultured according to the manufacturer's instructions after HPV exposure. The hours of operation of the HPV decontamination service were 8 AM–8 PM, Monday to Friday.

Data Management and Statistical Methods

All data were entered into an Excel (Microsoft Corporation, Redmond, Washington) database. Acquisition rates of MDROs (both separately and combined) were compared across the 3 cohorts. Raw incidence rates in each cohort were measured as the number of MDRO acquisitions per 1000 patient-days. Incidence rate ratios (IRRs) were estimated by Poisson generalized linear models, adjusting for hospital unit, age, mortality risk score, human immunodeficiency virus status, end-stage renal disease status, compliance with MDRO surveillance procedures, and calendar time. The analysis was performed using acquisitions of each of the 4 MDROs separately as the outcome and once using acquisition of any MDRO as the outcome.

Table 1. Demographic Characteristics of Study Patients

	No MDRO-Standard	MDRO-HPV	MDRO-Standard
Total room occupations	6709	600	1504
Unit 1 (HPV)	1232	109	70[b]
Unit 2 (HPV)	1695	366	429[b]
Unit 3 (HPV)	733	120	92[b]
Unit 4 (non-HPV)	1114	3[a]	244
Unit 5 (non-HPV)	883	1[a]	545
Unit 6 (non-HPV)	1052	1[a]	124
Total individuals	4817	500	1290
Mean age, y	57.2	54.6	55.6
Female, %	45.61	45.80	45.58
Race			
Caucasian, %	61.78	60.80	66.74
Black, %	31.33	31.00	36.51
Other, %	6.89	8.20	6.20
Comorbidities			
Diabetes, %	7.02	11.40	11.24
ESRD, %	12.81	31.20	21.40
HIV, %	1.76	0.80	3.26
Organ transplant, %	14.35	41.40	24.73
3M mortality risk score	3.0	2.7	3.2

Abbreviations: ESRD, end-stage renal disease; HIV, human immunodeficiency virus; HPV, hydrogen peroxide vapor; MDRO, multidrug-resistant organism.

[a] Five rooms on non-HPV units were decontaminated for infection prevention and control reasons during the study period. Patients admitted to these rooms were included in the MDRO-HPV cohort.

[b] These rooms were not able to be decontaminated using HPV for logistical reasons so were cleaned and disinfected using standard methods. Patients admitted to these rooms were included in the MDRO-standard cohort.

Statisticians who had not been involved in the clinical activities of the study performed the analysis. The Sweave package [30] in R, version 12.1 [31] was used.

The evaluation was approved by the Institutional Review Board of the Johns Hopkins University.

RESULTS

Overall, 8813 room occupations of ≥48 hours were included in the study (Figure 1); 1777 (20.2%) with a known history of an MDRO and 686 (7.8%) involved in a chlorhexidine study were excluded. Following exclusions, 6350 (72.0%) room occupations by 5378 patients were at risk of nosocomial MDRO acquisition (Figure 1). Patients at risk of acquiring 1 MDRO were not necessarily at risk of acquiring another MDRO, hence: 6936, 7514, 7928, and 8117 room occupations

Table 2. Summary of the Incidence of Acquisition, by Multidrug Resistant Organism (MDRO) and Cohort, and for all MDROs Combined

MDRO/Cohort	No.	Acquisitions, No.	Patient-Days, No.	Acquired, %	Crude IR per 1000 Patient-Days	Adj IRR[a]	95% CI	*P* Value
VRE	6936	333						
MDRO-standard	654	53	4566	8.1	11.6	…	…	…
No MDRO-standard	5808	272	37 973	4.7	7.2	0.85	(.61–1.18)	.32
MDRO-HPV	474	8	3267	1.7	2.4	0.25	(.10–.60)	<.01
MRSA	7514	121						
MDRO-standard	494	14	3736	2.8	3.7	…	…	…
No MDRO-standard	6463	102	44 931	1.6	2.3	0.62	(.33–1.17)	.13
MDRO-HPV	557	5	4010	0.9	1.2	0.53	(.16–1.79)	.30
MDR-GNR	8117	111						
MDRO-standard	1298	23	9928	1.8	2.3	…	…	…
No MDRO-standard	6235	81	43 092	1.3	1.9	0.81	(.48–1.34)	.40
MDRO-HPV	584	7	4225	1.2	1.7	0.55	(.20–1.57)	.26
Clostridium difficile	7928	130						
MDRO-standard	1253	26	9676	2.1	2.7	…	…	…
No MDRO-standard	6118	100	42 328	1.6	2.4	0.95	(.60–1.51)	.83
MDRO-HPV	557	4	4029	0.7	1.0	0.49	(.16–1.47)	.19
Combined	6350	497						
MDRO-standard	927	98	6228	10.6	15.7	…	…	…
No MDRO-standard	4986	381	30 119	7.6	12.6	0.9	(.70–1.16)	.40
MDRO-HPV	437	18	2904	4.1	6.2	0.36	(.19–.70)	<.01

Patients at risk of acquiring 1 MDRO may not be at risk of acquiring another MDRO, so the number of patients included for each MDRO varies.

Abbreviations: CI, confidence interval; GNR, gram-negative rod; HPV, hydrogen peroxide vapor; IR, incidence rate; IRR, incidence rate ratio; MDR, multidrug-resistant; MDRO-standard, patients admitted to a room where the prior room occupant had an MDRO and the room was cleaned and disinfected using standard methods; MDRO-HPV, patients admitted to a room where the prior room occupant had an MDRO and the room was decontaminated using HPV; MRSA, methicillin-resistant *Staphylococcus aureus*; No MDRO-standard, patients admitted to a room where the prior room occupant was not known to have an MDRO and the room was cleaned using standard methods; VRE, vancomycin-resistant enterococci.

[a] IRR was adjusted for potential confounders including unit, age, mortality risk score, HIV status, ESRD status, surveillance compliance of the unit (included in VRE and MRSA models) and time (using quarterly indicators);

were at risk of acquiring VRE, MRSA, *C. difficile*, and MDR-GNR, respectively.

Impact on MDRO Acquisition in Subsequent Room Occupants

Throughout the evaluation period, 497 of 6350 (7.8%) room occupations by patients without a history of an MDRO resulted in the acquisition of at least 1 MDRO; 333 of 6936 (4.8%) acquired VRE, 121 of 7514 (1.6%) acquired MRSA, 130 of 7928 (1.6%) acquired *C. difficile*, and 111 of 8117 (1.4%) acquired an MDR-GNR.

The patient demographics of the 3 cohorts were similar (Table 1). Patients admitted to rooms decontaminated using HPV (MDRO-HPV cohort) were significantly less likely to acquire any MDRO when compared with patients admitted to rooms cleaned and disinfected using standard methods (MDRO-standard cohort) before and after adjusting for possible confounders (adjusted IRR, 0.36; 95% confidence interval [CI], .19–.70; Table 2).

The significant reduction in MDRO acquisitions was mainly driven by the reduced incidence of VRE acquisition, which was approximately 5 times less likely in the MDRO-HPV cohort before and after adjusting for possible confounders (adjusted IRR, 0.20; 95% CI, .08–.52; Table 3).

The risk of acquisition was lower in the MDRO-HPV cohort than in the MDRO-standard cohort for MRSA, MDR-GNR, and *C. difficile*, although these differences were not statistically significant (Table 2). Restricting the analysis for VRE and MRSA to patients with an admission surveillance culture indicated that the differences in rates between the cohorts were similar to the full analysis; MDRO-standard vs MDRO-HPV for VRE was the only significant difference (IRR, 0.19; 95% CI, .05–.53; $P < .001$; data not shown). Reduced acquisition associated with HPV disinfection occurred independently of changes in rates on each unit and over time (Table 3). There were no significant changes in the rates of acquisition in the MDRO-standard and No MDRO-standard cohorts

Table 3. Adjusted Incidence Rate Ratio[a] of Vancomycin-Resistant Enterococci Acquisition by Exposure

	IRR	Lower	Upper	*P* Value
No MDRO-standard	0.76	0.56	1.04	.08
VRE-HPV	0.20	0.08	0.52	<.01
Other MDRO-HPV	0.33	0.10	1.10	.07
Age	1.01	1.00	1.01	.08
Mort Risk[b] 2	1.67	0.85	3.29	.13
Mort Risk 3	2.63	1.41	4.92	<.01
Mort Risk 4	4.26	2.27	7.99	<.01
HIV	1.94	1.04	3.63	.03
ESRD	1.23	0.93	1.62	.14
Compliance with admission surveillance cultures	0.72	0.56	0.94	.01

Abbreviations: ESRD, end-stage renal disease; HIV, human immunodeficiency virus; HPV, hydrogen peroxide vapor; IRR, incidence rate ratio; No MDRO-standard, patients admitted to a room when the prior room occupant was not known to have an MDRO and the room was cleaned using standard methods; VRE-HPV, patients admitted to a room when the prior room occupant had VRE and the room was decontaminated using HPV; Other MDRO-HPV, patients admitted to a room when the prior room occupant had *Clostridium difficile*, multidrug-resistant gram-negative rods, or methicillin-resistant *Staphylococcus aureus* and the room was decontaminated using HPV; VRE, vancomycin-resistant enterococci.

[a] Model was adjusted to take into account potential clustering within units and also included quarterly indicators; data not included in table. Exposure was compared to MDRO-standard for VRE.

[b]Mort Risk, risk of mortality as calculated by 3M APR-DRG software.

comparing the preintervention and intervention study phases on the HPV and non-HPV units (Table 4).

Environmental Findings

Overall, 218 (21.0%) of the 1039 patient rooms sampled were contaminated with ≥1 MDRO. The overall proportion of rooms contaminated with MDROs reduced significantly on the HPV units during the intervention phase, but not on the non-HPV units (relative risk [RR], 0.65; $P = .03$; Table 5). In particular, rooms contaminated with multiple MDROs (RR, 0.16; $P < .01$), MDROs cultured from a room that differed from the room occupant's known MDRO (RR, 0.37; $P = .01$), and MDROs cultured from empty rooms (RR, 0.31; $P = .05$) were less frequent on HPV units during the intervention phase (Table 5).

HPV Decontamination

Of the 8813 discharges during the entire study period, 1872 rooms housed patients with MDROs on HPV units during the intervention phase; 1334 (71.3%) of these were decontaminated using HPV, comprising 91.7% single-occupancy rooms. Two-thirds (n = 355) of the missed decontaminations occurred during hours when the HPV service was not available and 4.1% (n = 22) due to an urgent admission. Of the rooms decontaminated using HPV, 62.1%, 38.4%, 19.1%, and 10.5% had previously housed patients with VRE, MRSA, MDR-GNR, and *C. difficile*, respectively. There was no significant difference in the type of MDRO in HPV compared with missed decontaminations (data not shown).

One brand of paint used on the walls of one of the HPV units showed some incompatibility with the process; once this was replaced, there were no reports of damage to materials or equipment. No health and safety incidents were associated with HPV during the study. All biological indicators were inactivated. The technology was well accepted by unit staff (data not shown).

DISCUSSION

The role of environmental contamination in the transmission of healthcare-acquired pathogens is increasingly recognized [1–3, 7]. However, the best interventions to prevent transmission remain controversial because data on clinical outcomes are limited. We found that HPV decontamination decreased environmental contamination, particularly of rooms

Table 4. Multidrug Resistant Organism Acquisition by Cohort, Study Phase, and Unit

Cohort	Unit	Study Phase	IR/1000 Patient-Days	IRR	95% CI	*P* Value
MDRO-standard	Non-HPV units	Preintervention	16.1	…	…	…
		Intervention	13.5	0.83	(.50–1.43)	.47
	HPV units	Preintervention	14.0	…	…	…
		Intervention	12.7	0.91	(.48–1.70)	.75
No MDRO-standard	Non-HPV units	Preintervention	13.9	…	…	…
		Intervention	10.7	0.77	(.57–1.06)	.09
	HPV units	Preintervention	11.2	…	…	…
		Intervention	10.8	0.96	(.73–1.27)	.78

Abbreviations: CI, confidence interval; HPV, hydrogen peroxide vapor; IR, incidence rate; IRR, incidence rate ratio; MDRO, multidrug-resistant organism; No MDRO-standard, patients admitted to a room when the prior room occupant was not known to have an MDRO and the room was cleaned using standard methods.

Table 5. Environmental Sampling Results on the Hydrogen Peroxide Vapor (HPV) and Non-HPV Units in the Preintervention vs Intervention Phases

	HPV Units				Non-HPV Units			
	Preintervention Phase	Intervention Phase	RR	*P* Value	Preintervention Phase	Intervention Phase	RR	*P* Value
Total No. of rooms sampled	170	397			156	316		
Occupied rooms on precautions	49 (36.8)	101 (35.9)	0.98	.91	40 (35.7)	82 (41.8)	1.17	.33
Rooms contaminated with any MDRO	36 (21.2)	55 (13.9)	0.65	.03	37 (23.7)	90 (28.5)	1.20	.32
Multiple MDROs	8 (4.7)	3 (0.8)	0.16	<.01	4 (2.6)	10 (3.2)	1.23	1.00
VRE	16 (9.4)	35 (8.8)	0.94	.87	23 (14.7)	63 (19.9)	1.35	.20
MDR-GNR	8 (4.7)	9 (2.3)	0.48	.10	6 (3.8)	4 (1.3)	0.33	.09
MRSA	3 (1.8)	8 (2.0)	1.14	1.00	4 (2.6)	12 (3.8)	1.48	.60
C. difficile	1 (0.6)	0 (0.0)	0.00	.30	0 (0.0)	1 (0.3)	…	1.00
MDRO matches the current room occupant	14 (8.2)	37 (9.3)	1.13	.75	15 (9.6)	32 (10.1)	1.05	1.00
MDRO differs from the current room occupant	15 (8.8)	13 (3.3)	0.37	.01	18 (11.5)	39 (12.3)	1.07	.88
Contaminated empty rooms[a]	7 (4.1)	5 (1.3)	0.31	.05	5 (3.2)	19 (6.0)	1.88	.27
Contaminated communal sites	4 (14.8)	8 (14.8)	1.00	1.00	6 (22.2)	6 (11.1)	0.50	.20

Data are presented as No. (%).

Abbreviations: HPV, hydrogen peroxide vapor; MDR-GNR, multidrug-resistant gram-negative rod; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; RR, relative risk; VRE, vancomycin-resistant enterococci.

[a] Empty rooms are those that had been vacated, cleaned, and disinfected to be ready for the next admission.

contaminated with multiple MDROs, which may have survived from previous room occupants [4] and of empty rooms. Most importantly, we found that HPV used as an adjunct to a standard environmental cleaning and disinfection program reduced the risk of patient acquisition of MDROs by 64% in a large number of patients in busy, high-risk units. VRE, an organism with a known predilection for the environment [1, 6, 7], is endemic in our institution and was the organism most commonly isolated from the environment and most commonly acquired. Not surprisingly, VRE was the MDRO acquisition most markedly reduced by adjunctive HPV use in our institution. Comparison of the rates between the cohorts indicates that 28 MDRO transmissions were prevented by HPV on the 3 HPV units over the 18 months.

Recent findings that admission to a room where the prior room occupant was infected or colonized with an MDRO increases the risk of subsequent room occupant acquiring that MDRO provides compelling evidence that contaminated surfaces contribute to transmission [1, 6–9, 15]. Our findings extend these earlier studies, by showing that the risk from the prior room occupant is mitigated by effectively removing the environmental reservoir through the use of HPV decontamination [4, 19, 22]. Similarly, a recent study provides evidence that efforts to improve the efficacy of conventional cleaning and disinfection mitigated the increased risk of acquisition from an MRSA-colonized prior room occupant, but not from a VRE-colonized prior room occupant [15].

A surprising finding of our study was that HPV may protect patients even when the prior room occupant was not known to be colonized with an MDRO (ie, acquisition rates were lower in the MDRO-HPV cohort than in the No MDRO-standard cohort). Whether this was the result of unidentified MDRO carriers, residual contamination from previous room occupants, or contamination of healthcare workers' hands is not known [3, 6, 32]. Further work is required to explore this association.

MRSA, MDR-GNR, and *C. difficile* acquisitions were not independently reduced when HPV was used. We attribute these findings to the relatively low incidence of MDRO acquisition in a setting of enhanced focus on infection prevention and control strategies, including improved cleaning and disinfection of the environment [6–9, 15]. Therefore, whether HPV decontamination mitigates risk of acquisition conferred by a prior room occupant infected or colonized with MRSA, *C. difficile*, and MDR-GNRs should be investigated in more detail. Studies in endemic settings with a high incidence of acquisition of these pathogens or in outbreak settings will be helpful in addressing the impact of HPV on organisms besides VRE.

Regular use of HPV presents several practical challenges, including the need to vacate areas for the duration of the

decontamination and the need to seal air vents and doors. Importantly, the HPV service did not impact the day-to-day work of the staff. There were no safety, equipment, or ongoing material compatibility problems reported. We were able to decontaminate 71% of the rooms that met the criteria for HPV decontamination using 2 trained individuals with 2 suites of equipment from 8 PM to 8 AM 5 days per week. Only a small proportion (4.1%) of rooms that were vacated by patients with MDROs were not decontaminated owing to an urgent need to admit the next patient, which concurs with other findings [33].

Our study has several limitations. First, this is a single-institution study, so results may not be generalizable to other institutions that may have a different MDRO profile or lower acquisition rates. Second, neither rooms nor units were randomly assigned the intervention, which may have introduced bias. Third, as with many infection prevention studies, there were multiple infection prevention initiatives ongoing during the study period. In particular, another intervention, chlorhexidine daily bathing of patients, was introduced on some non-HPV units. While we attempted to control for this intervention by removing those patients receiving chlorhexidine baths from the analysis and this likely biased our results towards the null, we could not completely remove all impact. Fourth, while our analysis attempted to adjust for compliance with VRE and MRSA surveillance cultures, rates of compliance varied and improved during the study period in all units, potentially impacting our acquisition rates. Fifth, our environmental sampling methods did not quantify the contamination level, but the use of broth enrichment would have improved the sensitivity of the method [4]. Finally, given that some rooms were "missed" (ie, not decontaminated despite prior occupant known to have an MDRO) and the low prevalence of acquisition (especially for MDROs besides VRE), detecting changes in incidence was difficult. In settings with lower acquisition rates, a larger, multicenter trial would be necessary to show a significant impact.

In summary, HPV decontamination used as an adjunct to standard cleaning and disinfection reduced the risk of MDRO acquisition among high-risk patients when patients are admitted to a room previously occupied by a patient infected or colonized with an MDRO. These findings suggest that HPV should be considered for decontamination of MDRO patient rooms. Given the rising issue of resistant gram-negative organisms, the continued impact of other MDROs and a patient population that is increasingly susceptible to infection, strategies to optimally clean and disinfect the environment are essential. The results of our study, one of the few to evaluate not just environmental contamination but also patient outcomes, suggest that HPV in addition to a thorough infection prevention program should be implemented in high-risk environments to maximize patient safety.

Notes

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