ORIGINAL ARTICLE

Outbreak of Multidrug-Resistant *Pseudomonas aeruginosa* Colonization and Infection Secondary to Imperfect Intensive Care Unit Room Design

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BACKGROUND. *Pseudomonas aeruginosa* has been increasingly recognized for its ability to cause significant hospital-associated outbreaks, particularly since the emergence of multidrug-resistant strains. Biofilm formation allows the pathogen to persist in environmental reservoirs. Thus, multiple hospital room design elements, including sink placement and design, can impact nosocomial transmission of *P. aeruginosa* and other pathogens.

METHODS. From December 2004 through March 2006, 36 patients exposed to the intensive care unit or transplant units of a tertiary care hospital were infected with a multidrug-resistant strain of *P. aeruginosa*. All phenotypically similar isolates were examined for genetic relatedness by means of pulsed-field gel electrophoresis. Clinical characteristics of the affected patients were collected, and a detailed epidemiological and environmental investigation of potential sources was carried out.

RESULTS. Seventeen of the infected patients died within 3 months; for 12 (71%) of these patients, infection with the outbreak organism contributed to or directly caused death. The source of the outbreak was traced to hand hygiene sink drains, where biofilms containing viable organisms were found. Testing by use of a commercial fluorescent marker demonstrated that when the sink was used for handwashing, drain contents splashed at least 1 meter from the sink. Various attempts were made to disinfect the drains, but it was only when the sinks were renovated to prevent splashing onto surrounding areas that the outbreak was terminated.

CONCLUSION. This report highlights the importance of biofilms and of sink and patient room design in the propagation of an outbreak and suggests some strategies to reduce the risks associated with hospital sinks.

Infect Control Hosp Epidemiol 2009; 30:25-33

An important goal in hospital design is to create a safe environment for the delivery of patient care. While much attention is typically directed toward the potential dispersion of environmental organisms, such as *Aspergillus* and *Legionella* species, during construction activities, other pathogens, such as *Pseudomonas* and *Serratia* species, may also pose an ongoing hazard once the facility is operational. By advising on aspects of room design, patient placement, and plumbing facilities, infection control consultation can ensure that the risks of hospital-acquired infections are minimized.

Pseudomonas aeruginosa has been increasingly recognized for its ability to cause significant hospital-associated outbreaks of infection, particularly since the emergence of multidrug-resistant strains. Outbreaks of multidrug-resistant *P. aeruginosa* colonization or infection have been reported on urology wards, a burn unit, hematology/oncology units, and adult and neonatal critical care units.[1-8] Various medical devices and environmental reservoirs have been implicated in these outbreaks, including antiseptic solutions and lotions; endoscopy equipment; ventilator apparatus; and mouth swabs.[9-13] These sources can easily be eliminated once identified. A greater challenge exists if the source of an outbreak involves permanent components of the hospital physical plant, such as plumbing fixtures.

We describe an outbreak of multidrug-resistant *P. aeruginosa* infection that resulted from colonization of hand hygiene sink drains in a recently constructed tertiary care medical/surgical intensive care unit (MSICU), transplant stepdown unit, and transplant ward. This report highlights the key role of sink design and inpatient room design in causing such an outbreak, and it outlines effective strategies to manage outbreaks of this nature. We also emphasize the challenges that surround early outbreak recognition in a complex medical care facility.

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Received April 10, 2008; accepted August 6, 2008; electronically published December 1, 2008.

 0899-823X/2009/3001-0006$15.00. DOI: 10.1086/592700

METHODS

Outbreak Overview

The outbreak occurred from December 2004 through March 2006 and involved 3 hospital areas: the MSICU, the solid organ transplant stepdown unit, and the solid organ transplant ward. The outbreak strain of *P. aeruginosa* was phenotypically determined to be resistant to all antipseudomonal antibiotics (ie, ceftazidime, imipenem, ciprofloxacin, piperacillin-tazobactam, and gentamicin), except for variable sensitivity to amikacin.

Epidemiologic Investigation

Possible outbreak-affected patients were defined as patients admitted to the affected area during the outbreak period who were colonized or infected with *Pseudomonas* isolates that matched the outbreak phenotype. An epidemiologic investigation was carried out to search for potential case-case links or case–common environmental source links. Demographic and clinical information for affected patients was collected by means of retrospective review of electronic medical records and the laboratory information system. Environmental screening for the outbreak strain was performed on 8 occasions in the outbreak areas.

Microbiologic Evaluation of Clinical and Environmental Isolates

All specimens collected for culture and sensitivity testing were tested for antimicrobial susceptibilities, according to standard protocols.[14] The routine panel of antimicrobials tested by means of the VITEK automated instrument (bioMérieux) included ceftazidime, ciprofloxacin, gentamicin, tobramycin, piperacillin-tazobactam, amikacin, and imipenem. Additional testing of susceptibility to meropenem and colistin was performed using the E-test (AB Biodisk). No standard guidelines for interpretation of E-test susceptibility of *P. aeruginosa* to colistin are available; an isolate with an E-test minimum inhibitory concentration of no more than 4 ug/mL was considered susceptible, in keeping with published recommendations.[15]

Molecular Characterization

The initial determination of whether an isolate belonged to the outbreak strain was made on the basis of the antimicrobial resistance phenotype; pulsed-field gel electrophoresis (PFGE) was then used to determine genetic relatedness. Isolates were digested using the restriction enzyme *Spe*I, with a protocol run time of 20 hours and switch times of 5.35 seconds (Bio-Rad CHEF Mapper; Bio-Rad). Bionumerics software (Applied Maths) was used to determine phylogenetic relatedness, as the criteria previously developed by Tenover et al.[16] were found to be too discriminatory.

Biofilm Testing

Drain plugs from 3 sink traps were carefully rinsed with sterile water to remove nonattached cells, stained with the Live/Dead BacLight kit (Molecular Probes), and examined in a fully hydrated state using confocal laser scanning microscopy. Whole sink traps were also removed, sealed with trapped water left inside, and stored at room temperature for up to 6 weeks. Replicate sections of the traps were cut off at intervals of 2 weeks; at each interval, one-half of the samples were directly stained with BacLight and examined with confocal laser scanning microscopy, and the other half were flooded with a tryptic soy broth (diluted to a concentration of 1%) and incubated for 24 hours at room temperature to determine the persistence and viability of biofilm microcolonies.

Hand Hygiene Sink Evaluation

To determine whether sink drain contents were being dispersed onto surfaces outside of the drain itself, an emulsification of a commercially available fluorescent marker (Glow Germ) was injected deep into the drain cover of a MSICU hand hygiene sink. The faucet was then turned on and the water run for 15 seconds, while handwashing took place. With light eliminated from the room and all surfaces of the room covered with black paper, the area surrounding the sink was examined for evidence of fluorescent residue by use of a long-wave ultraviolet light source. In order to ensure that nonspecific fluorescence was absent, a pretest using the same protocol but without the fluorescent marker was performed.

Outbreak Control Measures

The following outbreak control measures were attempted: the use of contact precautions (wearing of gowns and gloves by healthcare workers and single room isolation of the patient) for all colonized or infected cases; staff education; enhanced environmental cleaning; disinfection of hand hygiene sink drains; closure of hand hygiene sinks; and renovation of hand hygiene sinks to prevent splashing of drain contents.

Setting

The Toronto General Hospital is part of the University Health Network and is located in Toronto, Ontario, Canada. It is a 400-bed tertiary care center and solid organ transplantation referral center for central and eastern Canada, performing over 400 transplants per year (lung, renal, liver, heart, and multivisceral). The MSICU consists of 22 single rooms and 1 semiprivate room; the percentage of beds occupied by transplant recipients is approximately 40%. Adjacent to the MSICU is a transplant stepdown unit, with 8 single beds, for patients who are transitioning from the MSICU to the transplant ward or vice versa. The transplant ward is located 3 floors directly below the MSICU and contains 39 beds (in 17 single and 11 semiprivate rooms).

A typical MSICU room layout is shown in Figure 1*A*. The

dedicated hand hygiene sink is approximately 1.3 meters from the head of the bed, and it is directly adjacent to the medication and sterile dressing preparatory area (Figure 1*B*). The sink is a wall-mounted, hands-free model with a shallow stainless steel bowl. The water spout was designed to flow water directly into the sink drain, without hitting the sides of the bowl (Figure 1*C*).

RESULTS

Patient Characteristics

The epidemiologic curve for the preoutbreak, outbreak, and postoutbreak periods is shown in Figure 2. From December 2004 to July 2006, there were 36 patients identified as infected or colonized with the outbreak strain of *P. aeruginosa.* Table 1 outlines the characteristics of affected patients and types of infections.

Two-thirds of affected patients (24 of 36) were considered infected with the outbreak strain, and 17 (47.2%) of the total cohort died. An independent chart review of all deaths in infected patients revealed that infection with the outbreak strain caused death in 5 (29.4%) and contributed to death in 7 (41.2%).

Twenty-one (58.3%) of affected patients were identified while in the MSICU, 5 (13.9%) in the transplant stepdown unit, 4 (11.1%) on the transplant ward, and 6 (16.7%) elsewhere in the hospital building. Of note, all of the patients identified elsewhere in the building had prior exposure to the MSICU, transplant stepdown unit, or transplant ward within the outbreak period. Thirty-four (94.4%) of affected patients

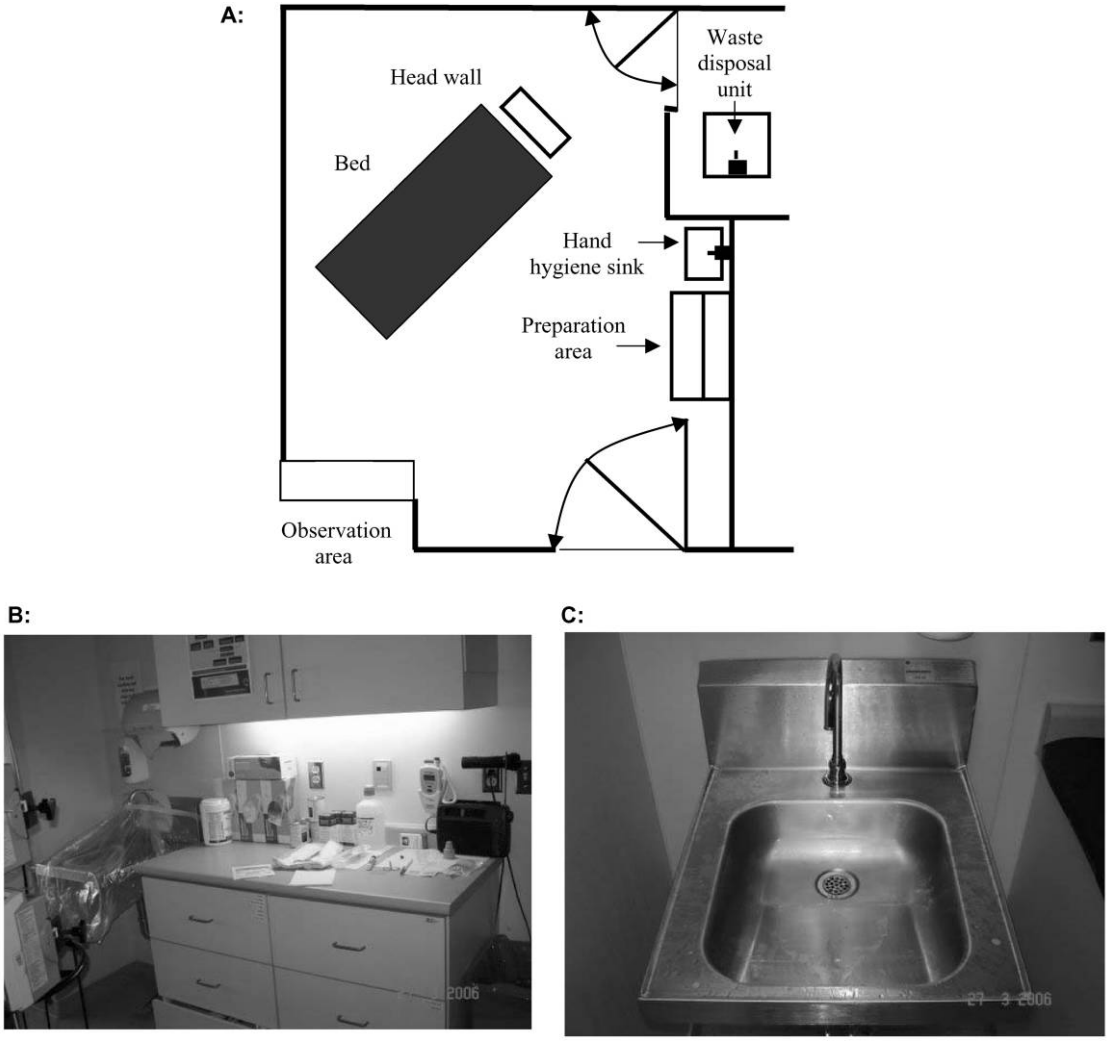

FIGURE 1. Three images from the medical surgical intensive care unit. *Panel A,* typical room layout; *panel B,* counter used for sterile procedures and medication preparation, in relation to sink; *panel C,* close-up of hand hygiene sink; note shallow bowl and gooseneck faucet.

were considered immunocompromised (by receipt of transplant, by malignancy, or by other cause).

Environmental Testing

A total of 288 environmental specimens were collected and analyzed for the presence of the outbreak strain; 28 specimens yielded positive results (Table 2). No multiuse equipment was found to be contaminated. Of all sources of environmental specimens, hand hygiene sink drains accounted for the highest proportions of positive culture results (11 of 65 sink drain specimens from the MSICU were positive for the outbreak strain, as were 10 of 59 sink drain specimens from the transplant stepdown unit and 5 of 89 sink drain specimens from the transplant ward). Many drains were found to be intermittently colonized. None of 39 specimens of source water tested yielded growth of *Pseudomonas* species. Two external plumbing fixtures were found to be positive (1 showerhead in the MSICU and 1 spout in the transplant stepdown unit).

Molecular Characterization

PFGE banding patterns for clinical and environmental isolates are presented in Figure 3. Two types, designated 1 and 16, were deemed sufficiently genetically related to be considered involved in the outbreak. The majority of clinical isolates were of PFGE type 1.

Biofilm Testing

Confocal laser scanning microscopy confirmed the presence of confluent biofilms, some areas more than 100 μm thick, in the samples analyzed (Figure 4). Viable multidrug-resistant *P. aeruginosa* isolates phenotypically consistent with the outbreak strain were recovered from these samples. Starvation experiments, in which the intact biofilms were kept for up to 6 weeks before addition of a dilute nutrient solution, showed that the biofilms rapidly responded: the relative abundance of viable cells in the biofilms more than doubled within 24 hours after nutrient addition.

Hand Hygiene Sink Evaluation

Tests using the fluorescent marker revealed that splashes originating from the drains of hand hygiene sinks were visible under fluorescence at least 1 m from the sink. We assume that microparticles not visible through fluorescence traveled further than 1 m. Most of the surfaces of adjacent medication and sterile dressing preparation areas were within the 1-m range.

Sink and Room Design Interventions

Disinfection of the hand hygiene sinks that yielded the outbreak strain was attempted on 2 separate occasions, as follows (Figure 2): a 7% accelerated hydrogen peroxide gel was

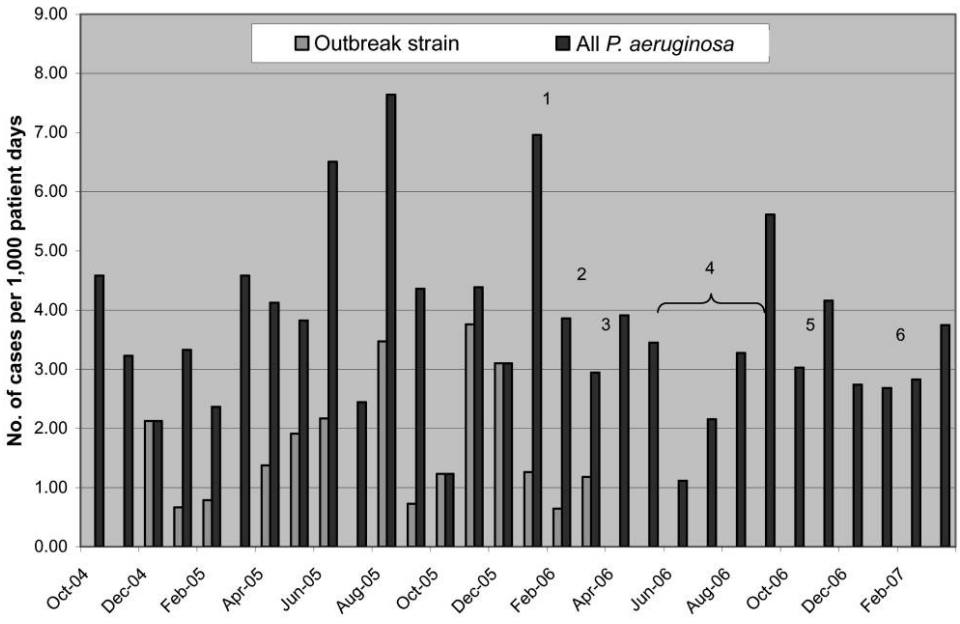

FIGURE 2. Epidemiologic curve showing the rate of colonization or infection with any strain of *Pseudomonas aeruginosa* and with the multidrug-resistant outbreak strain in the medical/surgical intensive care unit (MSICU) and transplant units, in relation to various sink and room design interventions. 1, sinks disinfected on 2 occasions, and sinks closed in MSICU and stepdown unit; 2, sinks opened in MSICU and transplant stepdown unit, and sinks in the 3 outbreak units closed and cleaned; 3, all sinks in outbreak units closed; 4, sinks renovated; 5, sinks opened in MSICU and transplant stepdown unit; 6, sinks opened in transplant ward.

TABLE 1. Characteristics of Cases in Outbreak of Multidrug-Resistant *Pseudomonas aeruginosa* Colonization and Infection Affecting 36 Patients

Variable	Value
Patient characteristic	
Age, years	
Mean ± SD	53.4 ± 14.3
Mean (range)	53.4 (19–80)
Male sex	19 (55.6)
Location of patient at recovery of first positive specimen	
MSICU	21 (58.3)
Transplant stepdown unit	5 (13.9)
Transplant ward	4 (11.1)
Other	6 (16.7)
Type of specimen yielding first positive result	
Sputum	17 (47.2)
Urine	7 (19.4)
Blood	5 (13.9)
Other[a]	7 (19.4)
Effect of pathogen on patient	
Colonization	12 (33.3)
Infection	24 (66.7)
Immunocompromised status	
Yes	
Due to solid organ transplant	21 (58.3)
Due to other immunosuppression	9 (25.0)
Due to cancer	4 (11.1)
No	2 (5.6)
Type of solid organ transplant received, no. (% of all transplants)	
Liver	8 (38.1)
Kidney	3 (14.3)
Lung	6 (28.6)
Heart	2 (9.5)
Multivisceral[b]	2 (9.5)
Underwent surgery prior to recovery of first positive specimen	17 (47.2)
Underwent invasive procedure prior to recovery of first positive specimen[c]	14 (38.9)
Death within 3 months of first positive specimen	17 (47.2)
Relation of multidrug-resistant *P. aeruginosa* infection to death	
Infection directly caused death	5 (29.4)
Infection contributed to death	7 (41.2)
Infection was unrelated to death	5 (29.4)
Duration of exposure to outbreak unit for all case patients, mean ± SD, days	34.2 ± 23.8
Isolate characteristic	
Resistant to amikacin	19 (52.8)
Susceptible to amikacin	17 (47.2)

NOTE. Data are no. (%) of patients, unless otherwise indicated. MSICU, medical surgical intensive care unit; SD, standard deviation.

[a] Percutaneous transhepatic cholangiography drain, wound, or catheter tip.

[b] One patient received a liver and lung transplant; 1 received a liver and short bowel transplant.

[c] Cystoscopy, endoscopy, bronchoscopy, tracheostomy, or chest tube insertion.

poured into sink drains and left for 5 minutes; sink surfaces, including the interior of faucet spouts, were exposed to a 1 : 16 dilution of the same product for 5 minutes. We submerged gooseneck faucets, drain strainers, and tap covers in 250 cc accelerated hydrogen peroxide 7% solution (diluted 1 : 16) for 5 minutes; wiped bowls with accelerated hydrogen peroxide 0.05% wipes; and closed MSICU and transplant stepdown unit patient room sinks. While sinks were closed, 2 additional attempts were made at cleaning drains of sinks with accelerated hydrogen peroxide 7% solution (diluted 1 : 16) gel product. Although postintervention cultures were sterile, several hand hygiene sinks became recolonized over time, and disinfection had no lasting impact on eradication of the outbreak strain. On the other hand, a decision to close

TABLE 2. Proportion (%) of Environmental Specimens Found Positive for the Outbreak Strain of *Pseudomonas aeruginosa,* by Hospital Unit

Source of specimen	Outbreak units				Other unit[a]
	MSICU	Stepdown unit	Transplant unit	All 3	
Sink taps and shower heads	1/27 (3.7)	1/16 (6.3)	0/10 (0.0)	2/53 (3.8)	…
Sink drains	11/65 (16.9)	10/59 (16.9)	5/89 (5.6)	26/213 (12.2)	…
Equipment[b]	0/16 (0.0)	0/4 (0.0)	0/2 (0.0)	0/22 (0.0)	0/5 (0.0)
Source water	…	…	…	0/19 (0.0)	0/20 (0.0)

NOTE. MSICU, medical/surgical intensive care unit.

[a] Cardiovascular intensive care unit or medical, surgical, or nephrology wards.

[b] Respiratory equipment, crash cart components, intravenous monitors, patient-lifting equipment, Pyxis medication-dispensing machine, multiple use fluid dispensers, ice machine, ultrasound gel, scissor hooks, and temperature probe.

all hand hygiene sinks in the outbreak areas corresponded with an immediate halt to identification of new cases. While closed, the sinks were renovated, as follows: traps were replaced; new faucet spouts were installed that did not flow directly into the drain, thereby minimizing splashback; water flow pressure was decreased; a barrier was installed between the sinks and adjacent preparatory areas (Figure 5); and patient care materials were moved move than 1 m from sinks. During this period, portable hand hygiene sinks and alcohol-based hand gel were used. After the sink modifications were complete, the fluorescent marker test for splash of drain contents was repeated on 1 intensive care unit sink; it revealed no splash onto the adjacent counter or patient bed.

DISCUSSION

We report a large outbreak of colonization and infection with multidrug-resistant *P. aeruginosa* that resulted in significant

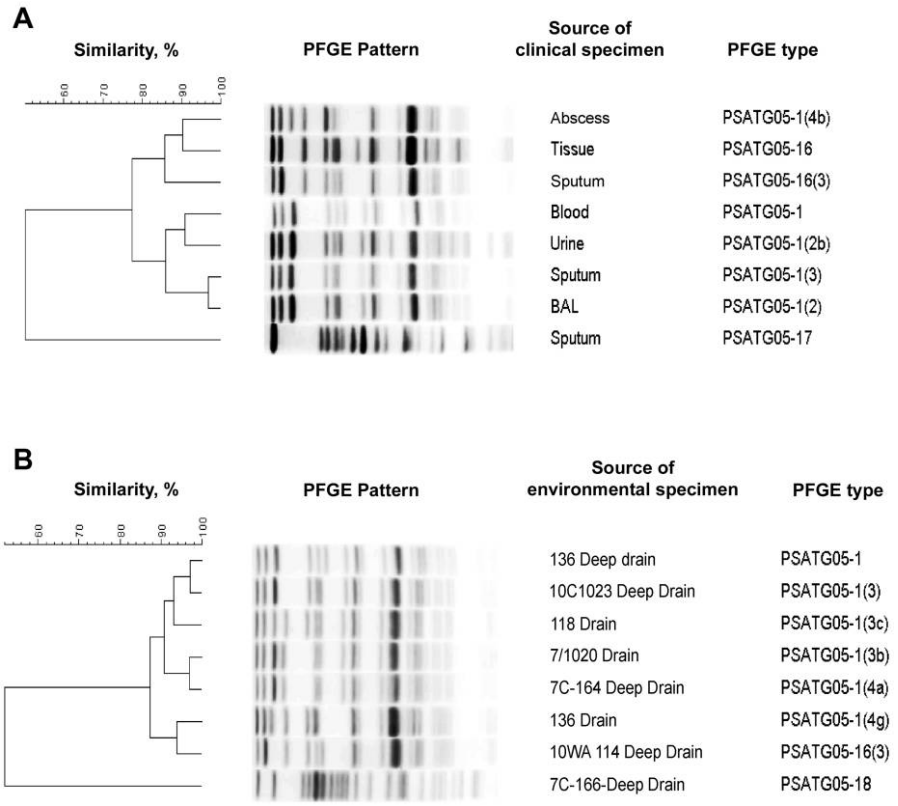

FIGURE 3. Banding patterns determined by pulsed-field gel electrophoresis (PFGE) and a dendrogram showing the genetic relatedness of isolates of multidrug-resistant *Pseudomonas aeruginosa* recovered from different patients and environmental sites. *Panel A,* clinical isolates; *panel B,* environmental isolates. BAL, bronchoalveolar lavage.

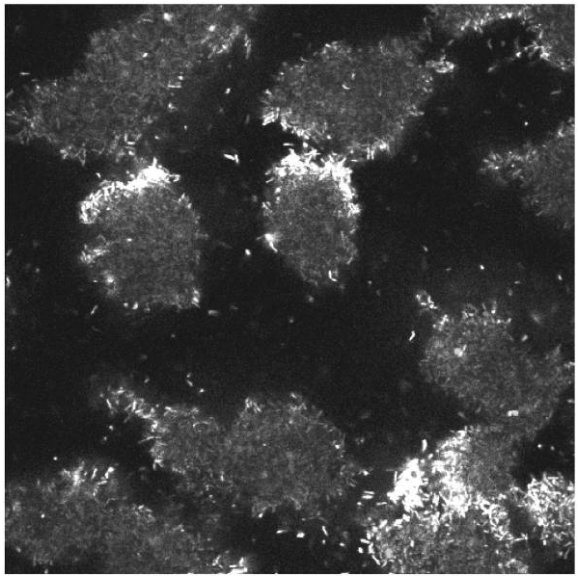

FIGURE 4. Confocal laser scanning micrograph showing biofilms containing microcolonies of the outbreak strain of *Pseudomonas aeruginosa*. Distance of optical thin section from attachment surface, 30 μm; original magnification, $\times$ 750.

morbidity and mortality in an immunocompromised population: 36 patients acquired the organism during an 18-month period, two-thirds of whom developed invasive infections. Of the 36 affected patients, 17 (47%) died, and 12 (71%) of these deaths were directly related either to the infection or to a subsequent complication. This high attributable mortality may be a reflection of the immunocompromised nature of the patient population, as well as the multidrug resistance and possible enhanced virulence of the outbreak strain.

This outbreak originated in hand hygiene sink drains. In conformity with current American Institute of Architects guidelines,[17] the MSICU was designed to have 1 hand hygiene sink installed per room; however, the outbreak investigation demonstrated that both the sink design and location were less than ideal. Sinks were situated sufficiently close to an area where sterile procedures and medication preparation were performed to presumably allow contamination of that area through the splash of drain contents. This risk was significantly reduced through the installation of splash barriers. The close proximity of the sink to the patient bed, while appropriate for point-of-care hand hygiene, likely enabled direct patient contamination. We assume that smaller, less visible particles traveled far further than the 1 m we were able to visualize using fluorescence.

We identified several issues with sink design on the affected units. Gooseneck faucets are a popular choice for hospital hand hygiene sinks because the faucet spout, when positioned the standard 10 inches (25.4 cm) above the bowl,[18] is high enough to minimize inadvertent touching of the bowl by utensils or hands. In our MSICU, the spout was fixed to flow water directly into the sink drain. In combination with high water pressure and a very shallow sink bowl, this created a means by which *Pseudomonas* biofilms within the drains could be disrupted, thereby transferring the viable organism to surrounding surfaces or, potentially, to the hands of healthcare workers.

Others have reported taps and drains as sources of outbreaks of *P. aeruginosa* colonization and infection.[1-4,6,7,19-25] These reports have been based on the sequential isolation of phenotypically or genotypically related strains from both sinks and clinical specimens, as in the present study.[19-22] *P. aeruginosa* was generally impossible to eradicate using disinfection techniques alone, and replacement of sinks or sink and/or plumbing components was emphasized as a means to eliminate the organism.[1-4,21,23] One group of investigators was able to successfully control an outbreak of infection with

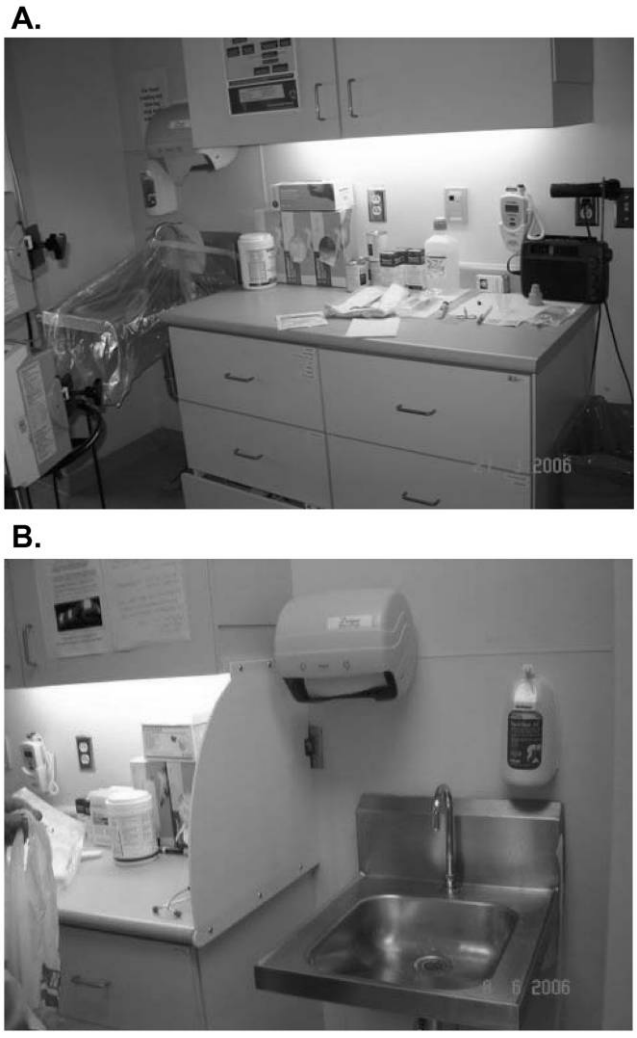

FIGURE 5. Sink and counter design in the medical/surgical intensive care unit where the outbreak occurred. *Panel A,* before renovation; *panel B,* after renovation.

multidrug-resistant *P. aeruginosa* by implementing pasteurization of water taps rather than the replacement of components[5]; however, tap colonization was only a late source of the organism in the outbreak (other sources were found earlier on environmental screening) and, thus, presumably had less opportunity to disseminate extensively. Also, environmental and clinical surveillance ended less than 2 months after the tap contamination was identified, so no long-term follow-up information was available.

In the present study, we visually demonstrated the probable mechanism of transfer of the outbreak organism to patients by means of the fluorescent marker testing. We also aborted the outbreak through simple sink and room design modifications to prevent splashing, without actually eradicating the organism or moving the sinks. We based this approach on the concept that biofilms are resistant to traditional disinfectant methods[26,27] and may, in fact, be more widespread than can be documented through visualization. The drains in our outbreak areas were proven to contain biofilms that tested positive for *P. aeruginosa*. These biofilms typically consist of a variety of microbial species that may protect pathogens from antimicrobials. Furthermore, our results showed the resilience and survival potential of biofilms under prolonged conditions of no water flow, which strongly suggest that biofilms can play an important role in recontamination or seeding. Replacing sinks and exposed piping would not eradicate biofilm that is more distal within the plumbing system; presumably this biofilm would simply recolonize new plumbing over time.

Identification of the outbreak was challenging on several levels. The background prevalence of patients colonized or infected with other multidrug-resistant *P. aeruginosa* strains made the cluster of outbreak cases less apparent. The continuous flow of patients between the 3 affected units, and the fact that many of these patients were close contacts of one another, made it challenging to determine the mechanism of acquisition of the outbreak strain.

A further delay resulted from difficulty in determining the relatedness of strains. Although the antibiogram pattern of the outbreak strain was relatively unique, it would occasionally change; similar antibiogram unpredictability of related strains of *P. aeruginosa* has been previously reported.[6,28] This made it challenging to identify possible cases requiring further investigation and PFGE typing; therefore, caution should be exercised in the use of phenotypic measures to determine relatedness. In addition, PFGE patterns frequently changed over time for both patient and environmental isolates; *P. aeruginosa* is known to mutate frequently, and isolates that would traditionally be considered genetically unrelated[16] may actually be from the same original clone.[28] Indeed, it was only after performing PFGE on many clinical and environmental isolates that we were able to identify 2 related families (types 1 and 16) of organisms that were in keeping with the clinical epidemiology of the outbreak.

Our renovations were successful in preventing the reemergence of infections with the outbreak strain. Follow-up environmental screening more than 1 year after the termination of the outbreak has shown that the organism persists in many drains in the outbreak area (data not shown); however, only 1 new infection has been identified on the previous outbreak units, in a patient at high risk, with large open wounds requiring extensive dressing changes.

In conclusion, our experience has demonstrated that, in addition to ensuring adequate numbers of hand hygiene sinks, sink placement and sink design are crucially important elements in the design of hospital rooms. This point becomes especially important in critical care areas, such as intensive care units.

ACKNOWLEDGMENTS

Financial support. Funding for this outbreak investigation and management was provided by internal sources (University Health Network).

Potential conflicts of interest. All authors report no conflicts of interest relevant to this article.

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