Successful Control of an Outbreak of *Klebsiella pneumoniae* Carbapenemase–Producing *K. pneumoniae* at a Long-Term Acute Care Hospital

L. Silvia Munoz-Price, MD; Mary K. Hayden, MD; Karen Lolans, BS; Sarah Won, MD; Karen Calvert, BS, MT(ASCP); Michael Lin, MD; Alexander Stemer, MD; Robert A. Weinstein, MD

**Objective.** To determine the effect of a bundle of infection control interventions on the horizontal transmission of *Klebsiella pneumoniae* carbapenemase (KPC)–producing *K. pneumoniae* during an outbreak.

**Design.** Quasi-experimental study.

**Setting.** Long-term acute care hospital.

**Intervention.** On July 23, 2008, a bundled intervention was implemented: daily 2% chlorhexidine gluconate baths for patients, enhanced environmental cleaning, surveillance cultures at admission, serial point prevalence surveillance (PPS), isolation precautions, and training of personnel. Baseline PPS was performed before the intervention was implemented. Any gram-negative rod isolate suspected of KPC production underwent a modified Hodge test and, if results were positive, confirmatory polymerase chain reaction testing. Clinical cases were defined to occur for patients whose samples yielded KPC-positive gram-negative rods in clinical cultures.

**Results.** Baseline PPS performed on June 17, 2008, showed a prevalence of colonization with KPC-producing isolates of 21% (8 of 39 patients screened). After implementation of the intervention, monthly PPS was performed 5 times, which showed prevalences of colonization with KPC-producing isolates of 12%, 5%, 3%, 0%, and 0% (*P* < .001). From January 1, 2008, until the intervention, 8 KPC-positive clinical cases—suspected to be due to horizontal transmission—were detected. From implementation of the intervention through December 31, 2008, only 2 KPC-positive clinical cases, both in August 2008, were detected. From January 1 through December 31, 2008, 8 patients were detected as carriers of KPC-producing isolates at admission to the institution, 4 patients before and 4 patients after the intervention.

**Conclusion.** A bundled intervention was successful in preventing horizontal spread of KPC-producing gram-negative rods in a long-term acute care hospital, despite ongoing admission of patients colonized with KPC producers.

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*Klebsiella pneumoniae* carbapenemase (KPC) enzymes are Ambler class A carbapenemas that were first found in *K. pneumoniae*. These enzymes have been identified in other gram-negative bacilli, including *Escherichia coli*, *Serratia marcescens*, *Enterobacter* species, *Salmonella* species, and *Pseudomonas aeruginosa*. KPCs confer resistance to a broad range of antimicrobial agents, including penicillins, cephalosporins, monobactams, and carbapenems; concomitant resistance to fluoroquinolones and aminoglycosides is common. The only antibiotics that retain a consistently high level of in vitro activity against KPC producers are the polymyxins.

The first KPC-producing isolate was described in North Carolina in 2001. Reports soon followed from other regions of the United States, mostly on the East Coast. During subsequent years, rapid spread and endemicity of KPC-producing strains in New York City area acute care hospitals was documented. More recently, long-term care facilities (nursing homes) have been implicated in outbreaks of KPC-producing *K. pneumoniae* along the East Coast. At the present time, KPC-producing isolates have been identified in countries worldwide, including Colombia, Israel, Greece, Brazil, France, and China.

In May 2008, the Rush University Medical Center clinical microbiology laboratory staff identified a KPC-producing *K. pneumoniae* isolate in a sample obtained from a patient who had been transferred from a hospital in neighboring northwest Indiana. This discovery—and the history of rapid spread of KPC-producing strains in other cities—quickly energized regional microbiology laboratories and infectious diseases specialists to determine the extent of the problem. Regional mi-
microbiology surveillance began to reveal KPC-producing *K. pneumoniae* isolates in multiple healthcare facilities in the southern suburbs of Chicago and in adjacent northwest Indiana; patients who were either infected or colonized with KPC-producing *K. pneumoniae* were identified in various acute care hospitals, post–acute care facilities, and nursing homes of the region. A long-term acute care hospital (LTACH) was identified as the epicenter of the outbreak.

LTACHs serve patients with complex medical needs and high device utilization rates; these patients require weaning from mechanical ventilation, hemodialysis, complex wound care, or long-term intravenous antibiotic therapy during long-term hospitalization in an acute setting. LTACHs are not nursing homes; patients admitted to these facilities are required by the Centers for Medicare and Medicaid Services to receive acute care and to have an average length of stay of at least 25 days. LTACHs have been described as “the perfect storm” for the development and spread of antibiotic resistance, because critically ill patients who are at risk for prior colonization with multidrug-resistant organisms from different acute care hospitals are clustered in the same location for long periods. This report describes a successful infection control intervention to control an outbreak of KPC-producing *K. pneumoniae* at an LTACH.

**METHODS**

This study was conducted during the period from January 1, 2008, through December 31, 2008, at a 70-bed LTACH in the greater Chicago area as part of an institutional infection control intervention.

**Setting**

The study facility is a 2-floor 70-bed LTACH with double-occupancy rooms that is located within a short-term acute care hospital (hospital-within-a-hospital model). Patients admitted to the facility include patients with tracheostomies who require weaning from mechanical ventilation and patients who require hemodialysis, intravenous antibiotics, or intensive care for complex wounds. Admitting coordinators tend to place patients with greater care needs in rooms on the lower floor and patients who are able to ambulate in rooms on the upper floor. The same nursing and ancillary staff, including respiratory therapists and cleaning personnel, work on both floors; during the outbreak, the same staff took care of both patients who were colonized with KPC-producing strains and patients who were not colonized. An on-site registered nurse functions as the institution’s full-time infection preventionist. During 2008, the mean length of stay at the facility was 25.3 days. The same year, a total of 566 patients were admitted, for a total of 14,246 patient-days, of which 3,385 (23.8%) were ventilator-days.

**Clinical Cases**

A clinical case was defined as occurring in a patient for whom a KPC-producing aerobic gram-negative rod was found in a clinical culture sample. Patients with clinical cases were identified prospectively during the period from May 13, 2008—the date when regional laboratories were alerted of the potential outbreak—through December 31, 2008. All gram-negative rod isolates identified during this period by use of the MicroScan Walkaway System (Siemens) that displayed intermediate susceptibility or resistance to imipenem or ertapenem were evaluated for KPC production. In addition, the electronic clinical microbiology database (LabPro Information Manager; Siemens Healthcare Diagnostics) was reviewed retrospectively to detect any previously unrecognized suspected cases in records from January 1, 2008, through May 12, 2008. Isolates identified by means of retrospective review were not available for additional testing.

**Colonized Cases**

Colonized cases occurred in patients who were identified as carriers of a KPC-producing aerobic gram-negative rod solely on the basis of surveillance culture results, either at admission or during point prevalence surveillance (PPS; see below).

**Microbiological Methods**

Beginning on May 13, 2008, any gram-negative rod isolate that was suspected of KPC production underwent a modified Hodge test. Each isolate that yielded a positive result with the modified Hodge test underwent KPC polymerase chain reaction (PCR) testing to confirm the presence of a KPC β-lactamase. Pulsed-field gel electrophoresis was performed on all available KPC-positive isolates according to the method of Matushek et al with use of XbaI (New England Biolabs), a voltage of 6 V/cm at 14°C for 21 hours, and pulse times linearly ramped from 5 to 35 seconds. Strain relatedness was determined according to the criteria of Tenover et al. Double rayon swabs in liquid Stuart transport medium (BBL CultureSwab; Becton Dickinson) were used to obtain culture samples from environmental sites in patient rooms. Swabs were inoculated directly onto plates of tryptic soy agar that contained 5% sheep’s blood.

**Bundled Intervention**

On July 23, 2008, a bundle of infection control interventions was instituted in an attempt to control the outbreak of KPC-producing *K. pneumoniae*. No antimicrobial stewardship program was in place during this outbreak, nor was antibiotic control included in the bundle.

*Daily chlorhexidine baths.* Daily chlorhexidine baths were performed for all patients as previously described. In brief, the institution’s pharmacy staff diluted bulk 4% chlorhexidine (Betasept; Purdue Pharma) to 2% in tap water. The 2% solution was then distributed to patient rooms in 1-gallon con-
tainers and restocked as needed. Nursing aides cleansed patients daily up to their jawlines with use of cotton washcloths saturated with the 2% solution; all body cavities were spared. Use of additional water or soap was avoided. During the intervention, the institution’s infection preventionist performed daily rounds to enforce the use of daily chlorhexidine baths. In addition, the pharmacy department provided regular reports of chlorhexidine use.

Environmental cleaning. Two cleaning personnel were identified as the only staff in charge of cleaning the facility on a daily basis. They were both observed while cleaning 4 rooms (2 each), including 2 postdischarge “terminal” cleanings. Several surfaces were observed not to be cleaned at all, including bed rails, intravenous pumps and poles, respiratory tubing systems, oxygen valves (attached to the walls), and call buttons. It was later discovered that a previous directive by the administration had placed registered nurses in charge of cleaning surfaces deemed to be close to patients (eg, bed rails and intravenous pumps and poles) in order to prevent accidental patient injury. Follow-up interviews with nurses revealed that nurses did not follow this rule.

On the basis of our observations, we continued to direct that cleaning be performed with use of quaternary ammonium products according to existing institutional policy. However, buckets were eliminated from all cleaning carts to lessen the possible risk of environmental cross-contamination between patient rooms, and use of spray bottles was instituted. Furthermore, cleaning personnel were authorized and expected to clean all surfaces, including bed rails and intravenous pumps and poles in close proximity to patients. Rooms of patients who were colonized with KPC-producing gram-negative rods were cleaned at the end of the day. The relevance of meticulous cleaning was emphasized on a one-on-one basis with both cleaning staff members during the initial visit and during 2 subsequent follow-up visits.

Respiratory therapists were assigned nightly cleaning of all mechanical ventilator surfaces and wall-mounted oxygen valves. Nursing aides were instructed to disinfect, with use of quaternary ammonium wipes (Sani Cloth HB; Nice-Pak Products), all objects shared among patients (eg, blood pressure machines and glucometers) after each use. Finally, because all bedside curtains (used for patient privacy) were found to be soiled, new curtains were installed on July 22, 2008.

Surveillance cultures. According to existing institutional policy, surveillance culture samples from the rectum, nares, wounds, central vascular catheter insertion sites, and gastronomy tube sites were collected within 24 hours from all newly admitted patients; however, as part of the bundled intervention, all ertapenem- or imipenem-nonsusceptible gram-negative rods identified in surveillance cultures were also evaluated for KPC production as described above.

PPS. We performed baseline PPS before the bundled intervention and follow-up PPS on 5 occasions. On PPS days, surveillance rectal swab culture samples were obtained from all patients in the institution (including patients who had been previously identified as carriers of KPC-producing strains) and evaluated for KPC-producing gram-negative rods.

Isolation and contact precautions. At admission, all patients considered to have high risk (ie, those patients on hemodialysis, with a tracheostomy, or with a history of colonization or infection with a multidrug-resistant organism, including a KPC-producing gram-negative rod) were placed under contact precautions (ie, use of gown and gloves by healthcare workers). Each isolation room for patients under contact precautions was supplied with its own disposable stethoscope, blood pressure cuff, and thermometer. Isolation and contact precautions were in place for high-risk patients until the results of all admission surveillance cultures were available. If culture results were negative, high-risk patients were kept under contact precautions but cohorted in double-occupancy rooms with other KPC-negative patients, unless the occupancy rate permitted a move to single-bed rooms. KPC-positive patients were also cohorted in double-occupancy rooms, if necessary on the basis of the institution’s occupancy rate, and maintained under contact precautions.

Patients considered not to be at high risk for colonization or infection with KPC-producing strains were not placed under contact precautions or isolation at admission, but they did participate in admission surveillance culture sampling. Patients newly identified as carriers of KPC-producing strains during PPS, or at any time during their hospital stay, were placed under contact precautions in private rooms or were cohorted in double-occupancy rooms.

Personnel education. Physicians, staff nurses, nursing aides, respiratory therapists, and hemodialysis nurses all received training on the relevance of KPC-producing gram-negative rods and their routes of transmission. Educational pamphlets were placed in high-traffic areas of the institution, including nursing stations, bathrooms, and staff lounges. Because several patients who were positive for KPC-producing strains required either mechanical ventilation or hemodialysis, special emphasis was placed on training respiratory therapists and hemodialysis nurses. In coordination with managers, we made sure that hemodialysis nurses’ personal objects (eg, cell phones, pages, clipboards, pens, food, books, and supply boxes) were not present during in-room dialysis, and the use of contact precautions was enforced during all dialysis treatments at the institution regardless of patient colonization status. Hemodialysis nurses were also trained to perform surface disinfection of their machines after every dialysis treatment at the institution.

Environmental cultures. Environmental cultures of 3 patient rooms, 2 of which were occupied by patients who were colonized or infected with a KPC-producing strain, were performed 1 week after implementation of the bundled intervention, which, as previously described, included coaching of cleaning personnel. Surfaces cultured included bed rails, me-
chanical ventilators, tubing systems, intravenous medication pumps and poles, hemodialysis machines, and bedside tables. Specimens were obtained before the scheduled daily cleaning.

Statistical analysis. We analyzed the change in point prevalence rates over time by using the exact calculation of the Cochran-Armitage test for trend. Analyses were performed with SAS 9.1.3 (SAS Institute).

RESULTS

Eleven LTACH patients with positive results on clinical cultures were identified during the outbreak (Figure 1); 10 were patients who had KPC-negative surveillance culture results at admission. The sources of positive clinical culture results were samples from 4 patients with bacteremia (1 primary bacteremia, 2 due to urinary tract infections, and 1 due to an infected decubitus ulcer), 2 patients with urinary tract infections, 2 patients with lower respiratory tract infections, 2 patients with wound infections, and 1 patient’s central vascular catheter tip. One patient was identified as a KPC carrier from a surveillance culture at admission (penile wound); KPC-producing *K. pneumoniae* was grown in cultures of sputum and urine samples collected 6 days after admission. Only 3 of the 11 clinical infections occurred after the implementation of the bundled intervention: 2 during the month of August (both patients had negative results on admission surveillance cultures) and 1 in December (the patient had a positive result on admission surveillance culture).

Eight patients were identified as carriers of KPC-producing strains at admission to the LTACH by means of surveillance cultures; body sites that tested positive with surveillance were the rectum (5 patients), wound sites only (2 patients), and both gastrostomy tube site and sacral decubitus ulcer site (1 patient). Patients who were positive for KPC producers at admission were detected at a similar frequency before and after implementation of the infection control bundle (Figure 1).

Baseline PPS of 39 patients that was performed 1 month before the start of the bundled intervention identified 8 (21%) patients who were positive for KPC-producing gram-negative rods (Figure 2). Two (25%) of the 8 patients who tested positive on surveillance had been identified previously as carriers of KPC-producing strains by means of admission surveillance cultures. After implementation of the bundled intervention, monthly PPS was performed 5 times (twice in September); rectal carriage of KPC-producing strains was found at a decreasing rate over the course of the intervention (Figure 2; *P < .001*). Among all KPC carriers identified during PPS, 6 subjects underwent PPS 2 or more times; 2 of these patients tested positive for KPC-producing strains twice.

All *K. pneumoniae* isolates identified were found to be related, with no more than a 6-band difference, according to the results of pulsed-field gel electrophoresis. Analysis of 4 isolates with DNA sequencing revealed *bla*<sub>KPC-3</sub>. In addition, we found 1 strain of *E. coli* and 1 strain of *Enterobacter aerogenes* in clinical cultures that were positive for KPC by PCR evaluation. No environmental culture samples yielded KPC-producing strains.

DISCUSSION

In this report, we describe the success of a bundled intervention in eliminating horizontal transmission of KPC-producing gram-negative rods at an LTACH, despite ongoing admission of patients colonized with KPC-producing bacteria. During 2008, regional microbiology surveillance revealed KPC-producing gram-negative rods in 25 acute and long-term care facilities in south suburban Chicago and northwest Indiana; KPC producers were previously unknown in this area. Because cases seemed to cluster at 1 LTACH—by June 2008, 8 of 18 cases were identified at this facility—baseline PPS was performed there, which revealed that 21% of LTACH patients were colonized with KPC-producing *K. pneumoniae*. Colonization pressure was further increased by ongoing admission of patients from acute care hospitals who were colonized with KPC-producing strains. Clinical cases occurred in patients who had negative results on surveillance cultures at admission, which suggests horizontal transmission within the facility (Figure 1).

The implementation of a bundle of interventions precludes determination of the effectiveness of any single measure. The infection control bundle covered 4 main aspects: decolonization of patients’ skin (with daily chlorhexidine baths), improved cleaning of environmental surfaces, identification of carriers of KPC-producing strains (with admission and surveillance cultures), and isolation (preemptive contact precautions and cohorting of high-risk patients at admission and on the basis of the results of clinical or surveillance cultures).

Surveillance cultures and isolation precautions have been recommended recently by the Centers for Disease Control and Prevention as interventions to control the spread of KPC-producing strains in the acute care setting. Our bundle included both of these interventions; therefore, we can only hypothesize about the individual effect of each. Cleansing the skin of colonized patients daily with 2% chlorhexidine gluconate has been shown in other studies to decrease the burden of vancomycin-resistant *Enterococcus* on patients’ skin, on healthcare workers’ hands, and on environmental surfaces. We hypothesized that these effects would also apply to KPC-producing *K. pneumoniae; Klebsiella* species have been shown to be transmitted by healthcare workers’ hands in previously reported outbreaks. Chlorhexidine baths had been used previously at this LTACH; however, their use was discontinued in October 2007. A formal assessment of compliance with isolation precautions and hand disinfection was precluded by a lack of personnel and overall limited resources; nevertheless, our experience during 5 years of infection control at the institution was that failure of healthcare workers to comply with isolation precautions was a common occurrence. Therefore, by decreasing the bacterial burden on patients’ skin and
outbreak of KPC-producing K. pneumoniae

FIGURE 1. Epidemiologic curve of patients colonized with *Klebsiella pneumoniae* carbapenemase (KPC)–producing gram-negative rods at a long-term acute care hospital. The monthly distribution of patients with KPC-positive clinical isolates or admission surveillance cultures is shown. January’s and April’s isolates were probable KPC producers (on the basis of phenotype); all other isolates were confirmed to produce KPC by means of polymerase chain reaction. Stars indicate 1 patient (depicted by these 2 rectangles) who was found to be a KPC carrier at admission and then 6 days later was found to have KPC-positive *Klebsiella pneumoniae* in clinical cultures of urine and sputum samples.

environmental surfaces, we could have decreased the potential contamination of healthcare workers’ hands during transgressions of isolation precautions, further decreasing horizontal transmission. In addition, an antimicrobial stewardship program was not implemented throughout this outbreak. The limitations of our study include its quasi-experimental nature and the lack of a postintervention phase; however, given the continuous influx of KPC-positive carriers to the institution from neighboring healthcare facilities, we decided that stopping the bundled intervention was not a viable op-

FIGURE 2. Results of point prevalence surveillance that was performed before and after the implementation of the bundle. On selected dates, rectal swab culture samples were obtained from all patients at the institution to determine carriage of *Klebsiella pneumoniae* carbapenemase (KPC)–producing gram-negative rods.
tion. Environmental cultures were not performed before the implementation of the bundle in order to prevent any further delay of the intervention; thus, we cannot assess the need for, or effect of, improved environmental cleaning. In addition, institutional budgetary constraints precluded the performance of patient skin cultures and healthcare worker hand cultures.

There are now approximately 400 LTACHs in the United States, mostly concentrated in urban areas and serving a sick patient population who undergo lengthy hospital stays. These institutions, despite serving as acute care hospitals, may lack the resources to keep a full staff of qualified nurses or a robust nurse-to-patient ratio. Nevertheless, we were able to demonstrate that even in this limited-resource environment it was possible to control the horizontal spread of KPC-producing strains despite the ongoing influx of colonized patients.

The role of LTACHs in regional outbreaks requires further research; however, on the basis of our preliminary results from the greater Chicago area, we can hypothesize that the “cycling” of patients colonized with KPC-producing strains through short-term acute care hospitals, LTACHs, and long-term care facilities (nursing homes) plays an important role in regional outbreaks and creates “resistance loops.” It is possible to control the horizontal spread of KPC-producing strains despite the ongoing influx of colonized patients.

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Address reprint requests to L. Silvia Munoz-Price, Jackson Memorial Hospital, Park Plaza West L-302, 1611 Northwest 12th Avenue, Miami, FL 33136-1096 (smunozprice@med.miami.edu).

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