# Prompt Control of an Outbreak Caused by Extended-Spectrum β-Lactamase–Producing *Klebsiella pneumoniae* in a Neonatal Intensive Care Unit

Joseph B. Cantey, MD[1], Pranavi Sreeramoju, MD[2,3], Mambarambath Jaleel, MD[1], Sylvia Treviño, MT[3], Rita Gander, PhD[4], Linda S. Hynan, PhD[5], Jennifer Hill, BSN[6], Cari Brown, BSN[6], Wendy Chung, MD, MPH[7], Jane D. Siegel, MD[1], and Pablo J. Sánchez, MD[1]

**Objectives** To assess the effectiveness of a set of multidisciplinary interventions aimed at limiting patient-to-patient transmission of extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* (ESBL-KP) during a neonatal intensive care unit (NICU) outbreak, and to identify risk factors associated with ESBL-KP colonization and disease in this setting.

**Study design** A 61-infant cohort present in the NICU during an outbreak of ESBL-KP from April 26, 2011, to May 16, 2011, was studied. Clinical characteristics were compared in infected/colonized infants and unaffected infants. A multidisciplinary team formulated an outbreak control plan that included (1) staff reeducation on recommended infection prevention measures; (2) auditing of hand hygiene and environmental services practices; (3) contact precautions; (4) cohorting of infants and staff; (5) alleviation of overcrowding; and (6) frequent NICU-wide screening cultures. Neither closure of the NICU nor culturing of health care personnel was instituted.

**Results** Eleven infants in this level III NICU were infected/colonized with ESBL-KP. The index case was an 18-day-old infant born at 25 weeks' gestation who developed septicemia from ESBL-KP. Two other infants in the same room developed sepsis from ESBL-KP within 48 hours; both expired. Implementation of various infection prevention strategies resulted in prompt control of the outbreak within 3 weeks. The ESBL-KP isolates presented a single clone that was distinct from ESBL-KP identified previously in other units. Being housed in the same room as the index infant was the only risk factor identified by logistic regression analysis ($P = .002$).

**Conclusion** This outbreak of ESBL-KP affected 11 infants and was associated with 2 deaths. Prompt control with eradication of the infecting strain from the NICU was achieved with multidisciplinary interventions based on standard infection prevention practices. *(J Pediatr 2013;163:672-79)*.

Outbreaks caused by multidrug-resistant organisms (MDROs) are a significant cause of morbidity and mortality in infants in neonatal intensive care units (NICUs) worldwide. Specifically, multidrug-resistant gram-negative bacilli, including extended-spectrum β-lactamase (ESBL)-producing organisms, have been responsible for an increasing number of NICU outbreaks,[1-3] resulting in worse outcomes, including death, in affected infants as well as higher health care costs.[4-7] When an outbreak is recognized in a NICU, prompt multidisciplinary investigation led by the infection prevention and control team and implementation of risk mitigation strategies are recommended.[8] Coordination and implementation of such control measures are often time-consuming and difficult, leading to ongoing transmission of the causative organism and occasionally necessitating closure of the unit to admissions.[9-11]

In 2011, an outbreak due to ESBL-producing *Klebsiella pneumoniae* (ESBL-KP) occurred in the NICU at Parkland Memorial Hospital (PMH) in Dallas. Here we report our multidisciplinary management of this outbreak, which resulted in the prompt control and eradication of this organism from the NICU, which remained open to all admissions. We also report our investigation of risk factors associated with ESBL-KP colonization and disease.

## Methods

PMH is a 672-bed public tertiary care center that provides a wide range of services, including high-risk obstetrics. The PMH NICU is a 90-bed level 3C,

| | |
|---|---|
| ESBL | Extended-spectrum β-lactamase |
| HCP | Health care personnel |
| KP | *Klebsiella pneumoniae* |
| MDROs | Multidrug-resistant organisms |
| NICU | Neonatal intensive care unit |
| PMH | Parkland Memorial Hospital |

From the Departments of [1]Pediatrics and [2]Internal Medicine, University of Texas Southwestern Medical Center; [3]Infection Prevention, Parkland Health and Hospital System; Departments of [4]Pathology and [5]Clinical Sciences, University of Texas Southwestern Medical Center; [6]Women and Infants' Specialty Health, Parkland Health and Hospital System; and [7]Dallas County Health and Human Services, Dallas, TX

The authors declare no conflicts of interest.

Presented in part at the Pediatric Academic Societies' Annual Meeting, Boston, MA, April 27 to May 1, 2012.

 http://dx.doi.org/10.1016/j.jpeds.2013.03.001

predominantly inborn unit with approximately 1200 admissions annually (Figure 1; available at www.jpeds.com). The NICU consists of 7 bays ("rooms" hereinafter) each with a maximum capacity of 12 infants depending on acuity (Figure 1, rooms A to G; Table I). There is 1 separate single bed, in a negatively ventilated isolation room (room H). A proximity-operated sink is located at the entrance to the NICU, and additional sinks are positioned at the entrance and rear of each room. Wall-mounted hand gel dispensers are available at the entrance to the NICU, at the entrance to each room, and at each bedside. Neither gowning nor a 3-minute surgical scrub is required for entrance into the NICU.

PMH's continuing-care nursery is an intermediate care unit on the same hospital floor but geographically separate from the main NICU area. It consists of 2 rooms with a maximum capacity of 10 infants per room (Table I, rooms I and J), and a separate, negatively ventilated isolation room capable of housing 3 infants. PMH's newborn nursery is a level-one nursery that spans 2 hospital floors and is geographically separate from both the continuing-care nursery and the NICU.

The study cohort comprised infants who were present in the NICU on the day of onset of illness in the index patient (April 26, 2011) and underwent at least 1 surveillance culture. The infants were followed to the time of hospital discharge or death. On May 2, 3 distinct infant cohorts, housed in separate rooms, were established: ESBL-KP–colonized infants, non–ESBL-KP–colonized infants who had been in the NICU when colonized infants were identified, and new admissions to the NICU after the outbreak was recognized. These latter infants who were admitted to the NICU after cohorting began on May 2 were not included in our study cohort. We defined a case as an infant in the NICU in whom ESBL-KP was isolated from bacterial cultures obtained from normally sterile sites (eg, blood, cerebrospinal fluid, urine), clinical samples taken from nonsterile sites (eg, tracheal aspirates, conjunctiva), or rectal/throat swab cultures obtained for surveillance.

On May 3, a multidisciplinary team was formed consisting of neonatologists (1 of whom was the medical director of the NICU), pediatric infectious disease physicians, the nurse director, nurse managers, respiratory therapy managers, medical director of infection prevention and control, infection preventionists, microbiologists, and the director of environmental services. On May 13, epidemiologists from the Dallas County Health and Human Services and the Texas Department of Health and Human Services were invited to assist the NICU multidisciplinary team with management and analysis.

Clinical cultures were obtained from infants at the discretion of the health care personnel (HCP). A schedule for obtaining surveillance cultures was initiated on May 2, 2011, after recognition of the outbreak. Rectal and throat swab cultures were obtained from each infant present in the NICU between May 2 and May 20; subsequently, only rectal swab cultures were obtained twice-weekly between May 20 and June 13, weekly between June 13 and August 1, and every other week thereafter, continuing to August 2012. The last infant in the cohort was discharged on September 9, 2011.

Specimens were processed in PMH's microbiology laboratory by plating samples onto MacConkey agar containing ceftazidime to select for $\beta$-lactamase production. ESBL-KP isolates were analyzed for relatedness with the DiversiLab *Klebsiella* DNA Fingerprinting Kit (bioMérieux, Durham, North Carolina).[12] Isolates were also sent to the Texas Department of Health and Human Services and the Centers for Disease Control and Prevention for confirmatory testing by pulsed-field gel electrophoresis.[13] The specific ESBL enzymes were identified by high-fidelity amplification polymerase chain reaction (5′ Prime, Gaithersburg, Maryland), as described previously.[14,15]

We conducted a cohort study to identify risk factors associated with ESBL-KP colonization or infection among all infants present in the NICU at any time between April 26 and May 2, 2011. Demographic, clinical, laboratory, and outcome data were collected for each infant in the cohort. Other data collected included daily room assignments, medical staff assignments, duration of invasive devices (eg, endotracheal tube for mechanical ventilation, central venous catheter), duration of parenteral nutrition, duration and type of enteral nutrition, surgical procedures performed in the operating room or at the bedside, radiographic studies, ophthalmology examinations, medication use (including surfactant, acid-blocking therapy, and antibiotics), transfusions of blood products, length of NICU stay, number and type of infections, and mortality. The number of ESBL-KP patient-exposure days was calculated by multiplying the number of days in any given room by the number of infected or colonized infants in that room; for example, being in the same room with 3 colonized infants for 4 days would equal 12 patient-exposure days.

Data are reported as median and IQR were provided for continuous measures, and infected or colonized infants were compared with uninfected infants using Mann-Whitney *U* statistics. Data are reported as number and percentage for categorical measures, and the $\chi^2$ test was used to compare the infant groups except where noted. Multivariate logistic regression using the forward stepwise method was used to predict infection group using demographic characteristics. The Hosmer-Lemeshow goodness-of-fit *P* value was used to describe the fit of the model to the data, with $P > .40$ considered to indicate a good fit. The variables included in the stepwise model were gestational age in days, birth weight, days of humidity, days in a bassinet, days with an umbilical arterial catheter in place, days with an umbilical venous catheter in place, days with a peripherally inserted central catheter in place, days of room air, number of abdominal ultrasound examinations, doses of surfactant received, days admitted to room E, and number of patient-exposure days. SPSS version 19 (IBM, Armonk, New York) and StatXact-8 (Cytel, Cambridge, Massachusetts) were used to analyze the data. All tests were 2-sided, with $P < .05$ considered to indicate significance.