



# A Cluster of Carbapenemase-Producing *Enterobacter cloacae* ST171 at a Tertiary Care Center Demonstrating an Ongoing Regional Threat



Minnesota Department of Health

Edwin C. Pereira, MD  
420 Delaware St SE, MMC 250  
Minneapolis, MN 55455  
pere0051@umn.edu

Edwin C. Pereira, MD<sup>1</sup>, Melissa Hargreaves, PhD<sup>2</sup>, Jeana Houseman, MHSA, DLM (ASCP), CIC<sup>3</sup>, Timothy Johnson, PhD<sup>4</sup>, Ruth Lynfield, MD, FIDSA<sup>5</sup>, Paula Snippes Vagnone, MT (ASCP)<sup>2</sup>, Medora Witwer, MPH<sup>5</sup>, and Susan Kline, MD, MPH, FSHEA<sup>1</sup>

<sup>1</sup>Division of Infectious Diseases and International Medicine, University of Minnesota, Minneapolis, MN, <sup>2</sup>Public Health Laboratory, Minnesota Department of Health, St. Paul, MN, <sup>3</sup>Infection Prevention, University of Minnesota Medical Center, Minneapolis, MN, <sup>4</sup>University of Minnesota, St. Paul, MN, <sup>5</sup>Minnesota Department of Health, St. Paul, MN

## Abstract

**Background:** Increasing prevalence of carbapenemase-producing (CP) bacteria represents an urgent public health threat. In MN and ND a clonal strain of *bla*<sub>KPC-3</sub>-producing *E. cloacae* has been reported with increasing frequency.

**Methods:** Between July 2015 and February 2016, 13 carbapenem-resistant *E. cloacae* isolates were identified at the University of Minnesota Medical Center (UMMC) and submitted to the MN Dept. of Health for *bla*<sub>KPC-3</sub>/*bla*<sub>NDM-1</sub> PCR; 5 *bla*<sub>KPC-3</sub> positive isolates were further characterized by PFGE and whole genome sequencing (WGS). Medical records of patients with CP-*E. cloacae* were reviewed.

**Results:** Five patients were hospitalized at UMMC. Patients A and B were hospitalized on the same unit 6 days apart. Patient A was hospitalized again 13 days prior to patient D, in the same room. Patients C and D were hospitalized on the same unit simultaneously. Patients C and E had previous hospitalizations in ND.

All 5 case-isolates were sequence type ST171 and *bla*<sub>KPC-3</sub> positive; 3 PFGE patterns with >90% similarity were identified (Figure 2). In addition, plasmid types and resistance genes were very similar between the isolates, although some differences were noted (Table). WGS showed isolates A, B, and D to be closely related with <10 SNP differences. Isolates C and E were closely related to each other, more distantly to A, B, and D; all belonged to the clonal lineage of the major circulating strain in MN and ND.

**Conclusion:** All 5 case-isolates were related, however there were some distinguishing features between the most closely related isolates (A/D, C/E) suggesting that there may not have been transmission between these patients at the time of their hospitalization at UMMC. Notably, the 2 case-isolates from ND patients were more similar than the 3 from MN. This report highlights the importance of using both epidemiological and molecular data. However, more experience with WGS and plasmid exchange is needed to fully understand the relationships revealed through molecular data.

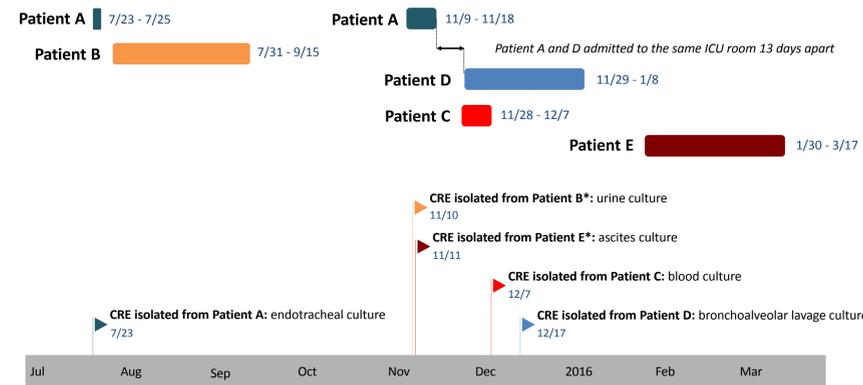
## Background

- Carbapenemase-producing (CP) bacteria represent a public health threat.
- The prevalence of CP bacteria has been increasing since the identification of the *Klebsiella pneumoniae* carbapenemase (KPC) in 2001.<sup>1,2</sup>
- In the US, KPC is the most commonly identified carbapenemase.
- A circulating strain of clonal *Enterobacter cloacae* carrying KPC has been identified in Minnesota and North Dakota.<sup>3,4</sup>
- The University of Minnesota Medical Center (UMMC) is an 847-bed tertiary-care hospital receiving many referrals from North Dakota (ND).
- The Minnesota Department of Health (MDH) conducts state-wide surveillance of carbapenem-resistant Gram-negative bacteria.

## Methods

- Between July 2015 and February 2016, 13 carbapenem-resistant *E. cloacae* isolates were identified at UMMC and sent to MDH.
- Five of 13 isolates were KPC producers. These five isolates were further characterized using PFGE typing and whole genome sequencing (WGS).
- Medical records of 5 patients with CP-*E. cloacae* were reviewed.

## Hospital Admission Timeline



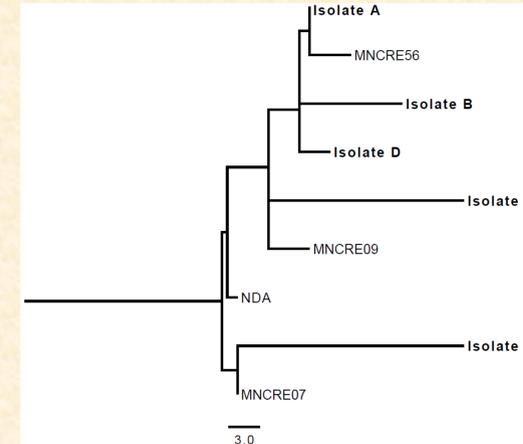
**Figure 1: Hospital admission timeline for five patients with carbapenemase-producing *E. cloacae* CRE – Carbapenem Resistant Enterobacteriaceae**  
\*Cultures not collected during UMMC hospitalization



**Figure 2: Dendrogram and PFGE patterns of five *E. cloacae* ST171 isolates**

Isolate	PFGE Pattern	Plasmid Types		Resistance Genes				
		IncFIA (HI1)	IncX3	<i>aadA1, strA, aacA4, strB, sul2, dfxA14, aac(6)'Ib-Cr, bla<sub>OXA-9'</sub>, bla<sub>TEM-1A'</sub></i>	<i>bla<sub>KPC-3'</sub></i>	<i>aph(3')-Ia</i>	<i>aph(3')-Ic</i>	<i>bla<sub>SHV-12'</sub></i>
A	ECL64	X		X	X	X		
B	ECL74	X	X	X	X	X		X
C	ECL18	X	X	X	X	X		X
D	ECL64	X		X	X		X	
E	ECL18	X		X	X	X		

**Table: Characteristics of five *E. cloacae* isolates**



**Figure 3: Dendrogram of the genetic relationship between the five *E. cloacae* isolates**  
Bar = 3 single nucleotide polymorphisms  
MNCRE56, MNCRE09, MNCRE07, and NDA refer to *E. cloacae* isolates previously reported as a clonal circulating strain.<sup>3,4</sup>

## Results

- Clinical Results
  - All 5 patients (A-E) with CP-*E. cloacae* had inpatient stays at UMMC (Figure 1).
  - Isolates from patients A-E were obtained from endotracheal, urine, blood, bronchoalveolar lavage, and ascites cultures, respectively.
  - Patients A and B were hospitalized on the same unit 6 days apart.
  - Patient A was hospitalized a second time, being discharged a few days prior to hospitalizations for patients C and D. Patients A and D occupied the same ICU room 13 days apart.
  - Patients C and D were concurrently hospitalized in the same ICU, overlapping for 9 days. Both patients expired during this hospitalization.
  - Patients C and E were both from ND. Patient C was transferred directly from a ND hospital to UMMC. Patient E was hospitalized at a separate ND hospital 2 months prior to the UMMC hospitalization.
- Laboratory Results
  - After patients C and D were identified to be KPC-positive, screening cultures from rectal and tracheal samples were obtained on all intubated patients in two adjacent ICUs (total 15 patients). All screening cultures were negative.
  - All five isolates (A-E) were found to be sequence type ST171.
  - Three different PFGE patterns were identified – all with >90% similarity (Figure 2).
  - WGS showed isolates A, B, and D to be closely related with <10 SNP differences. Isolates C and E were closely related, more distantly related to A, B, and D (Figure 3).
  - Plasmid types and resistance genes were very similar, but not identical, between isolates (Table). All were positive for the *bla*<sub>KPC-3</sub> gene.
  - All isolates belonged to the clonal lineage of the major circulating strain in Minnesota and North Dakota.

## Conclusions

- A clonal strain of CP-*E. cloacae*, matching a previously reported strain of ST171, has been identified in 5 patients at our institution.
- Clinical similarities in the identified patients were suggestive of possible transmission in the hospital, however distinguishing features identified following PFGE and WGS analyses raise questions of whether acquisition occurred from another source.
- Using both clinical and molecular data are important in evaluating clusters of similar isolates, however more experience with these techniques is needed to understand the relationships revealed with these data.

## References

1. Yigit H, Queenan AM, Anderson GJ, et al. Novel carbapenem-hydrolyzing beta-lactamase, KPC-1, from a carbapenem-resistant strain of *Klebsiella pneumoniae*. *Antimicrob Agents Chemother*. 2001;45(4):1151-1161.
2. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. *Clin Infect Dis*. 2011;53(1):60-67.
3. Hargreaves ML, Shaw KM, Dobbins G, et al. Clonal Dissemination of *Enterobacter cloacae* Harboring blaKPC-3 in the Upper Midwestern United States. *Antimicrob Agents Chemother*. 2015;59(12):7723-7734.
4. Kiedrowski LM, Guerrero DM, Perez F, et al. Carbapenem-resistant *Enterobacter cloacae* isolates producing KPC-3, North Dakota, USA. *Emerg Infect Dis*. 2014;20(9):1583-1585.



UNIVERSITY OF MINNESOTA  
Driven to Discover<sup>SM</sup>