

Notes from the Field

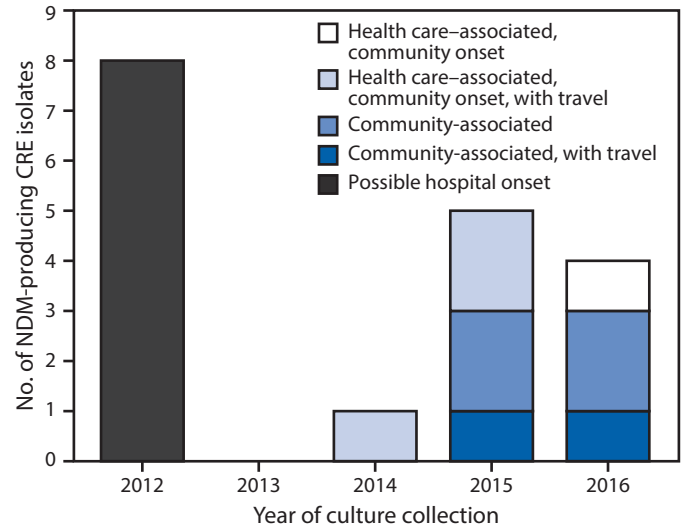
New Delhi Metallo- β -Lactamase–Producing Carbapenem-Resistant Enterobacteriaceae Identified in Patients Without Known Health Care Risk Factors — Colorado, 2014–2016

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Carbapenem-resistant Enterobacteriaceae (CRE) are considered an urgent threat in the United States because they are associated with high morbidity and mortality, limited treatment options, and potential for rapid spread among patients (1). Carbapenemases, enzymes that confer resistance to the carbapenem class of antibiotics, are believed to contribute to increasing transmission and regional spread of CRE because the genes encoding these enzymes can reside on mobile plasmids and can be transferred among bacterial species. *Klebsiella pneumoniae* carbapenemase (KPC) is the most common carbapenemase seen in the United States, but isolates with the New Delhi metallo- β -lactamase (NDM) are emerging. Known risk factors for carbapenemase-producing CRE, including NDM, include health care exposures such as hospitalization outside the United States, recent overnight admissions to short-stay and long-term acute care hospitals, residence in long-term care facilities, surgical procedures, and having indwelling devices. Community-associated CRE lack these health care exposures and are rare in the United States (2). During 2014–2016, NDM-producing CRE were isolated from patients in Colorado without known health care risk factors.

The Colorado Department of Public Health and Environment (CDPHE) has conducted statewide laboratory-based surveillance of CRE since November 2012. CRE isolates that are resistant to two or more carbapenems are tested for the KPC and NDM genes by polymerase-chain reaction at the CDPHE laboratory. As of April 2016, Colorado had reported the second highest number of NDM-producing CRE in the United States (3). NDM was first detected in Colorado in 2012 in eight patients during a hospital outbreak (4). Ten additional patients with NDM-producing CRE were identified in Colorado during 2014–2016. Among these 10 patients, the mean age was 64 years (range = 20–85 years); isolates from nine patients were from urine, and in one patient, from bile. Five patients had traveled internationally in the 2 months before specimen collection (two of whom had known hospitalizations during international travel) (Figure). In six patients, the isolate was detected from cultures collected in outpatient settings and

FIGURE. Number of identified CRE isolates that produce NDM, by epidemiologic classification* — Colorado, 2012–2016



Abbreviations: CRE = carbapenem-resistant Enterobacteriaceae; NDM = New Delhi metallo- β -lactamase.

* **Community-associated:** no known health care exposures, including hospitalizations, long-term care facility residence, surgery, dialysis, or indwelling devices. **Travel:** to international areas where the prevalence of NDM is unknown. **Health care-associated:** history of hospitalization, surgery, dialysis, indwelling devices, or residence in a long-term care facility in the year preceding the first known CRE-positive culture. **Possible hospital onset:** symptoms associated with the NDM isolate had onset >3 calendar days after hospital admission. The first known CRE-positive culture was detected during hospitalization; prior CRE colonization in patients is unknown.

lacked the known CRE risk factors of overnight stays in health care settings, dialysis, or surgery in the preceding 12 months, and had no invasive devices in the preceding 2 days (i.e., the isolates were community-associated).

Among the six patients identified with community-associated, NDM-producing CRE, two patients traveled internationally: one to an unknown country in Africa and one to the Bahamas. Mean age was 61 years (range = 20–85 years). All patients received diagnoses of urinary tract infections. Medical record review indicated that three of these six patients had antibiotic exposure, two within 1 month and the other within 10 months prior to the positive culture. Three of the six patients with community-associated, NDM-producing CRE had no underlying comorbidities; one patient was pregnant at the time of her positive culture, and two patients had underlying medical conditions. One patient with underlying medical conditions reported caring for a family member in multiple health care facilities before the positive NDM culture, including an acute care hospital, a long-term acute care hospital, and an assisted living facility.

There were no known epidemiologic links among the 10 most recent patients, and no known epidemiologic links between recent patients and patients from the 2012 outbreak. Whole genome sequencing (WGS) performed at CDC on isolates from 15 patients* confirmed that the recent isolates did not share common strains or plasmids with the 2012 outbreak. Among the seven recent isolates that underwent WGS, only two *E. coli* ST167 isolates appeared to be related. These isolates were separated by only 10 single nucleotide polymorphism differences and share a common NDM allele (*bla_{NDM7}*) and other genetic signatures; the two patients associated with these isolates resided in the same large metropolitan area but had no known epidemiologic links. The source for the community-associated strains is unknown, but might represent transmission of multiple NDM strains outside inpatient health care settings.

The vast majority of CRE isolates previously identified in Colorado were reported from patients with recent health care exposures or indwelling devices and with underlying comorbidities. Approximately 8% of the patients with CRE reported to CDC's Emerging Infections Program, which includes the Denver metropolitan area, did not have health care risk factors documented in their medical records; 9% did not have any underlying comorbidities (2). Of note, identification of carbapenemase-producing CRE from healthy international travelers without health care exposure has been reported (5); however, only two of the six patients with community-associated, NDM-producing CRE in Colorado had this exposure. The finding that six of 10 recent NDM-producing CRE are community-associated suggests that the epidemiology of CRE could be changing. Further surveillance is required to determine whether this pattern continues.

*The 15 patients include eight from the 2012 outbreak and seven more recent patients; DNA sequences were placed in the National Center for Biotechnology Information Sequence Read Archive under BioProject accession PRJNA328506 for the 2012 outbreak, and BioProject accession PRJNA328507 for the recent isolates.

Testing for common carbapenemases at clinical or state health laboratories can inform CRE epidemiology and guide health care facilities to implement additional infection prevention and control interventions, such as screening contacts of patients with a CRE infection or colonization (6). As a result of this investigation, CDPHE has now implemented patient interviews as a routine part of NDM-producing CRE case investigations to assist in determining possible risk factors and epidemiologic links.

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References

1. CDC. Antibiotic resistance threats in the United States, 2013. Atlanta, GA: US Department of Health and Human Services, CDC; 2014. <http://www.cdc.gov/drugresistance/threat-report-2013/>
2. Guh AY, Bulens SN, Mu Y, et al. Epidemiology of carbapenem-resistant Enterobacteriaceae in 7 US communities, 2012–2013. *JAMA* 2015;314:1479–87. <http://dx.doi.org/10.1001/jama.2015.12480>
3. CDC. Tracking CRE. Atlanta, GA: US Department of Health and Human Services, CDC; 2016. <http://www.cdc.gov/hai/organisms/cre/TrackingCRE.html>
4. Epton EE, Pisney LM, Wendt JM, et al. Carbapenem-resistant *Klebsiella pneumoniae* producing New Delhi metallo- β -lactamase at an acute care hospital, Colorado, 2012. *Infect Control Hosp Epidemiol* 2014;35:390–7. <http://dx.doi.org/10.1086/675607>
5. Ruppé E, Armand-Lefèvre L, Estellat C, et al. Acquisition of carbapenemase-producing Enterobacteriaceae by healthy travellers to India, France, February 2012 to March 2013. *Euro Surveill* 2014;19:20768. <http://dx.doi.org/10.2807/1560-7917.ES2014.19.14.20768>
6. CDC. Facility guidance for control of carbapenem-resistant Enterobacteriaceae (CRE)—November 2015 update CRE toolkit. Atlanta, GA: US Department of Health and Human Services, CDC; 2015.