Carbapenemase-Producing Enterobacteriaceae and Nonfermentative Bacteria, the Philippines, 2013–2016

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During 2013–2016, we isolated blaNDM-1 and blaVIM-harboring Enterobacteriaceae and nonfermentative bacteria from patients in the Philippines. Of 130 carbapenem-resistant isolates tested, 45 were Carba NP–positive; 43 harbored blaNDM-1 and 2 harbored blaVIM. Multidrug-resistant microbial pathogen surveillance and antimicrobial drug stewardship are needed to prevent further spread of New Delhi metallo-β-lactamase variants.

Carbapenemase-producing Enterobacteriaceae can efficiently hydrolyze carbapenems and most β-lactam drugs. Since the identification of New Delhi metallo-β-lactamase-1 (NDM-1) in 2008 (1), there has been great concern regarding the spread of the Ambler class B metallo-β-lactamases (MBLs). Confirmed infections with MBL-positive bacteria are rarely identified in the Philippines, but blaIMP-harboring Enterobacteriaceae were reported in 2014 (2), an Escherichia coli (sequence type [ST] 131) isolate harboring blaNDM-1 was reported in 2014 (3), and 2 Klebsiella pneumoniae (ST626 and ST903) isolates harboring blaNDM-1 and blaNDM-7 genes were reported in 2016 (4).

We performed isolate identification and antimicrobial drug susceptibility testing by using the MicroScan WalkAway 40 plus System (Beckman Coulter, Brea, CA, USA) on 1,516 gram-positive and gram-negative isolates from patients admitted to various wards in the V. Luna Medical Center, a tertiary-care military hospital in Manila, the Philippines, during August 2013–April 2016. To better assess the distribution of carbapenem resistance and the underlying molecular mechanisms of resistance, we selected gram-negative isolates with imipenem or meropenem (or both) MICs of ≥8 μg/mL. We used microbroth dilution susceptibility testing (5) to select and verify 130 gram-negative nonrepeat isolates (i.e., each isolate was tested once) and then tested the isolates for carbapenemase production by using the Carba NP test as previously described (6). We tested all isolates with a Carba NP–positive result for blaNDM and blaKPC by using a multiplex real-time PCR assay as previously described (7,8); isolates with PCR-negative results were further tested, using the Xpert Carba-R PCR test with the GeneXpert IV System (both from Cepheid, Sunnyvale, CA, USA), for the presence of blaNDM, blaKPC, blaVIM, blaIMP, and blaOXA-48.

Of the 130 bacterial isolates tested, 45 (35%) had positive Carba NP test results and 43 (33%) harbored blaNDM-1. 25 (58%) of the blaNDM-1-carrying isolates were identified as K. pneumoniae (online Technical Appendix Table, https://wwwnc.cdc.gov/EID/article/23/9/16-1237-Techapp1.pdf). None of the isolates was positive for blaKPC. Two Pseudomonas aeruginosa isolates that had positive Carba NP test results were negative for blaNDM-1 and blaKPC but positive for blaVIM. During the collection period, we also tested 8 environmental samples collected from the hospital’s neonatal intensive care unit and obstetrics and gynecology wards; 3 (38%) of the 8 isolates were positive for blaNDM and identified as K. pneumoniae (online Technical Appendix Table).

We report the identification of blaNDM-positive bacterial isolates in several genera of Enterobacteriaceae and nonfermentative bacteria in the Philippines. This finding is particularly significant because NDM-like enzymes have a broad range of activity against most β-lactam antimicrobial drugs and are often associated with serious clinical infections (9). A higher risk for plasmid-mediated transfer of NDM-1 exists through conjugation between different gram-negative bacterial strains (10), and NDM-1 can spread rapidly via nosocomial transmission or community-acquired infection. Furthermore, although limited in number, the environmental samples in this study were also positive for blaVIM, which suggests the possibility of nosocomial transmission and local circulation.

We conducted multiplex real-time PCR testing only for blaNDM, blaKPC, blaVIM, blaIMP, and blaOXA-48 and did not investigate clonality; thus, further investigation into other carbapenemase genes should be conducted. In addition, further experiments should be performed to characterize the plasmids carrying the carbapenemase genes. Strengthening of multidrug-resistant microbial pathogen surveillance and antimicrobial drug stewardship is urgently needed to better characterize drug-resistance patterns and improve early detection and containment strategies in developing countries.
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Chronic Wasting Disease Prion Strain Emergence and Host Range Expansion

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Chronic wasting disease (CWD) is a contagious prion disease of cervids that is spreading globally. CWD is enzootic in multiple cervid species, including deer and elk; the major foci of disease are Colorado/Wyoming (USA), Wisconsin/Illinois (USA), and Alberta/Saskatchewan (Canada). CWD is also present in captive cervids in South Korea and wild reindeer and moose in Norway (https://www.mwhc.usgs.gov/images/cwd/cwd_map.jpg). CWD results from the conformational transformation of the host-encoded cellular prion protein (PrPC) into protease-resistant, detergent-insoluble, β-sheet rich, amyloidogenic conformers, termed prions (PrPSC). Within their conformation, prion strains encapsulate the information that directs the templated misfolding and aggregation of PrPC molecules into additional prions (1).

Although the sequence homology of PrP among mammals is high, the ability of particular prion strains to cause disease in different species is determined by the conformational compatibility between a given strain and the host PrPC (2). We

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## Technical Appendix

**Technical Appendix Table.** Molecular resistance mechanisms of carbapenem-resistant clinical (n = 45) and environmental isolates (n = 3) from a tertiary-care military hospital in Manila, the Philippines, August 2013–April 2016*

| Identification | Source             | Organism     | Carba NP | blaNDM | blaKPC | blaOXM | Month | Year  | Imipenem MIC (µg/mL) | Meropenem MIC (µg/mL) | Sex | Hospital ward     |
|----------------|--------------------|--------------|----------|--------|--------|--------|-------|-------|----------------------|-----------------------|-----|-------------------|
| PH-0138–14     | Blood              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Nov   | 2013  | >8                   | >8                    | M   | Neonatal ICU     |
| PH-0542–14     | Soft tissue        | *E. coli*    | Pos      | Pos    | Neg    | ND     | Jun   | 2014  | >8                   | >8                    | M   | Pediatric        |
| PH-0630–14     | Wound              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jul   | 2014  | >8                   | >8                    | F   | Female Medical   |
| PH-0631–14     | Blood              | *C. freundii* | Pos      | Pos    | Neg    | ND     | Jul   | 2014  | >8                   | >8                    | M   | Neurosurgery    |
| PH-0756–14     | Catheter           | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Aug   | 2014  | >8                   | >8                    | F   | Medical ICU     |
| PH-0787–14     | Endotracheal tip   | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Aug   | 2014  | >8                   | >8                    | M   | Medical ICU     |
| PH-0837–14     | Catheter           | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Sep   | 2014  | >8                   | >8                    | F   | Female Surgical |
| PH-0846–14     | Catheter           | *E. cloacae*  | Pos      | Pos    | Neg    | ND     | Sep   | 2014  | >8                   | >8                    | M   | Male Medical     |
| PH-0850–14     | Urine              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Sep   | 2014  | >8                   | >8                    | F   | Female Medical   |
| PH-0873–14     | Urine              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Oct   | 2014  | >8                   | >8                    | M   | Surgical ICU     |
| PH-0874–14     | Wound              | Klebsiella sp. | Pos      | Pos    | Neg    | ND     | Oct   | 2014  | >8                   | >8                    | M   | Female Medical   |
| PH-0901–14     | Wound              | *C. freundii* | Pos      | Pos    | Neg    | ND     | Oct   | 2014  | >8                   | >8                    | F   | Female Surgical |
| PH-1037–14     | Catheter           | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Dec   | 2014  | >8                   | >8                    | F   | Female Medical   |
| PH-1076–14     | Urine              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Dec   | 2014  | >8                   | >8                    | M   | Medical ICU     |
| PH-1078–14     | Blood              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Dec   | 2014  | >8                   | >8                    | F   | Female Medical   |
| PH-1088–14     | Endotracheal tip   | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | F   | Medical ICU     |
| PH-1093–14     | Tracheal aspirate  | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Dec   | 2014  | >8                   | >8                    | F   | Female Medical   |
| PH-1099–14     | Endotracheal tip   | Acinetobacter sp. | Pos    | Pos    | Neg    | ND     | Dec   | 2014  | *                   | >8                    | M   | Surgical ICU     |
| PH-1115–14     | Blood              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Dec   | 2014  | >8                   | >8                    | F   | Female Medical   |
| PH-1142–15     | Blood              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | M   | Female Medical   |
| PH-1143–15     | Wound              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | M   | Neurology        |
| PH-1150–15     | Catheter           | *E. cloacae*  | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | M   | Neurosurgery     |
| PH-1159–15     | Catheter           | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | M   | Neurology        |
| PH-1165–15     | Urine              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | M   | Pulmonary Disease|
| PH-1166–15     | Urine              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Feb   | 2015  | >8                   | >8                    | M   | Surgical ICU     |
| PH-1261–15     | Blood              | *C. freundii* | Pos      | Pos    | Neg    | ND     | Jul   | 2015  | 8                    | >8                    | M   | Nephrology       |
| PH-1263–15     | Blood              | *E. cloacae*  | Pos      | Pos    | Neg    | ND     | Jul   | 2015  | >8                   | >8                    | F   | Neonatal ICU    |
| PH-1265–15     | Blood              | *E. cloacae*  | Pos      | Pos    | Neg    | ND     | Jul   | 2015  | 8                    | >8                    | F   | Neonatal ICU    |
| PH-1266–15     | Blood              | *E. cloacae*  | Pos      | Pos    | Neg    | ND     | Jul   | 2015  | >8                   | >8                    | F   | Neonatal ICU    |
| PH-1270–15     | Blood              | *K. pneumoniae* | Pos      | Pos    | Neg    | ND     | Jan   | 2015  | >8                   | >8                    | F   | Female Medical   |

*PH: Philippines. *Page 1 of 2
| Identification  | Source   | Organism    | Carba NP | bla_NDM | bla_KPC | bla_VIM | Month | Year | Imipenem MIC (µg/mL) | Meropenem MIC (µg/mL) | Sex | Hospital ward |
|-----------------|---------|-------------|---------|---------|---------|---------|-------|------|----------------------|-----------------------|-----|---------------|
| PH-1279-15      | Wound   | *K. oxytoca* | Pos     | Pos     | Neg     | ND      | Jan   | 2015 | 8                    | >8                    | M   | Neurology      |
| PH-1280-15      | Urine   | *C. freundii* | Pos     | Pos     | Neg     | ND      | Jan   | 2015 | >8                   | >8                    | M   | Neurology      |
| PH-1363-15      | Wound   | *P. aeruginosa* | Pos     | Pos     | Neg     | ND      | Sep   | 2015 | >8                   | >8                    | M   | Surgical ICU   |
| PH-1379-15      | Blood   | *K. pneumoniae* | Pos     | Pos     | Neg     | ND      | Sep   | 2015 | >8                   | >8                    | M   | Medical ICU    |
| PH-1384-15      | Blood   | *K. pneumoniae* | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | F   | Medical ICU    |
| PH-1394-15      | Wound   | *K. pneumoniae* | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | M   | Surgical ICU   |
| PH-1419-15      | Urine   | *K. pneumoniae* | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | F   | Female Medical |
| PH-1477-15      | Wound   | *E. cloacae*  | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | F   | Medical ICU    |
| PH-1478-15      | Wound   | *E. cloacae*  | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | F   | Female Medical |
| PH-1482-15      | Wound   | *K. pneumoniae* | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | F   | Medical ICU    |
| PH-1499-15      | Wound   | *E. cloacae*  | Pos     | Pos     | Neg     | ND      | Oct   | 2015 | >8                   | >8                    | F   | Medical ICU    |
| PH-1595-16      | Blood   | *E. cloacae*  | Pos     | Pos     | Neg     | ND      | Jan   | 2016 | >8                   | >8                    | F   | Female Medical |
| PH-1641-16      | Blood   | *K. pneumoniae* | Pos     | Pos     | Neg     | ND      | Feb   | 2016 | >8                   | >8                    | M   | Neurology      |
| PH-0745-14      | Wound   | *P. aeruginosa* | Pos     | Neg     | Neg     | Pos    | Aug   | 2014 | 8                    | >8                    | M   | Male Surgical  |
| PH-0905-14      | Soft tissue | *P. aeruginosa* | Pos     | Neg     | Neg     | Pos    | Oct   | 2014 | >8                   | >8                    | M   | Post-anesthesia Care Unit |

ATCC strains

| ATCC 2473 | *K. pneumoniae* | Pos | Pos | Neg | ND | Apr | 2016 |
| ATCC 1705 | *K. pneumoniae* | Pos | Neg | Pos | ND | Apr | 2016 |
| ATCC 1706 | *K. pneumoniae* | Neg | Neg | Neg | ND | Apr | 2016 |

Environmental isolates bla_NDM positive (n = 3)

| E1          | Laryngoscope | *K. pneumoniae* | Neg | Pos | Neg | ND | Nov | 2014 | >8 | >8 | Neonatal ICU |
| E3          | Incubator    | *K. pneumoniae* | Neg | Pos | Neg | ND | Nov | 2014 | >8 | >8 | Neonatal ICU |
| E7          | Suction 1    | *K. pneumoniae* | Neg | Pos | Neg | ND | Nov | 2014 | >8 | >8 | Neonatal ICU |

*ICU, intensive care unit; ND, not done; Neg, negative; Pos, positive.