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

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During 2013–2016, we isolated *bla*$_{NDM}$- and *bla*$_{VIM}$-harboring *Enterobacteriaceae* and nonfermentative bacteria from patients in the Philippines. Of 130 carbapenem-resistant isolates tested, 45 were Carba NP–positive; 43 harbored *bla*$_{NDM}$, and 2 harbored *bla*$_{VIM}$. 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 *bla*$_{IMP}$-harboring *Enterobacteriaceae* were reported in 2014 (*2*), an *Escherichia coli* (sequence type [ST] 131) isolate harboring *bla*$_{NDM-1}$ was reported in 2014 (*3*), and 2 *Klebsiella pneumoniae* (ST626 and ST903) isolates harboring *bla*$_{NDM-1}$ and *bla*$_{NDM-7}$ 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 *bla*$_{NDM}$ and *bla*$_{KPC}$ 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 *bla*$_{NDM}$, *bla*$_{KPC}$, *bla*$_{VIM}$, *bla*$_{IMP-1}$, and *bla*$_{OXA-48}$.

Of the 130 bacterial isolates tested, 45 (35%) had positive Carba NP test results and 43 (33%) harbored *bla*$_{NDM}$; 25 (58%) of the *bla*$_{NDM}$-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 *bla*$_{KPC}$. Two *Pseudomonas aeruginosa* isolates that had positive Carba NP test results were negative for *bla*$_{NDM}$ and *bla*$_{KPC}$ but positive for *bla*$_{VIM}$. 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 *bla*$_{NDM}$ and identified as *K. pneumoniae* (online Technical Appendix Table).

We report the identification of *bla*$_{NDM}$-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 *bla*$_{NDM}$, which suggests the possibility of nosocomial transmission and local circulation.

We conducted multiplex real-time PCR testing only for *bla*$_{NDM}$, *bla*$_{KPC}$, *bla*$_{VIM}$, *bla*$_{IMP-1}$, and *bla*$_{OXA-48}$ 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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Human and mouse prion proteins share a structural motif that regulates resistance to common chronic wasting disease (CWD) prion strains. Successful transmission of an emergent strain of CWD prion, H95^{+}, into mice resulted in infection. Thus, emergent CWD prion strains may have higher zoonotic potential than common strains.

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.nwhc.usgs.gov/images/cwd/cwd_map.jpg). CWD results from the conformational transformation of the host-encoded cellular prion protein (PrP^{C}) into protease-resistant, detergent-insoluble, β-sheet rich, amyloidogenic conformers, termed prions (PrP^{CWD}). Within their conformation, prion strains encipher the information that directs the templated misfolding and aggregation of PrP^{C} 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 PrP^{C} (*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	*bla*$_{NDM}$	*bla*$_{KPC}$	*bla*$_{VIM}$	Month	Year	Imipenem MIC (μg/mL)	Meropenem MIC (μg/mL)	Sex	Hospital ward
Patient isolates												
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 Oncology
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	F	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

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.