

## New Delhi Metallo- $\beta$ -Lactamase-5-Producing *Escherichia coli* in Companion Animals, United States

Stephen D. Cole, Laura Peak, Gregory H. Tyson, Renate Reimschuessel, Olgica Ceric, Shelley C. Rankin

Author affiliations: University of Pennsylvania School of Veterinary Medicine, Philadelphia, Pennsylvania, USA (S.D. Cole, S.C. Rankin); Louisiana State University, Baton Rouge, Louisiana, USA (L. Peak); US Food and Drug Administration, Silver Spring, Maryland, USA (G.H. Tyson, R. Reimschuessel, O. Ceric)

DOI: <https://doi.org/10.3201/eid2602.191221>

We report isolation of a New Delhi metallo- $\beta$ -lactamase-5-producing carbapenem-resistant *Escherichia coli* sequence type 167 from companion animals in the United States. Reports of carbapenem-resistant *Enterobacteriaceae* in companion animals are rare. We describe a unique cluster of *bla*<sub>NDM-5</sub>-producing *E. coli* in a veterinary hospital.

Carbapenems are critically useful antimicrobial drugs that are reserved for treatment of infections caused by multidrug-resistant, gram-negative bacteria (1). Carbapenem-resistant *Enterobacteriaceae* (CRE) have emerged as a major cause of human healthcare-associated infections and are a major clinical and public health problem (1). The most common mechanism of resistance is production of carbapenemases, which hydrolyze carbapenems and many other  $\beta$ -lactams. The genes that encode carbapenemases are found on conjugative plasmids and commonly fall in the following classes: KPC (*Klebsiella pneumoniae* carbapenemase), NDM (New Delhi metallo- $\beta$ -lactamase), IMP (imipenemase), and VIM (Verona integron-encoded metallo- $\beta$ -lactamase) (1). Control of these infections in human healthcare settings is a challenge because the organisms colonize the gastrointestinal tract and can go undetected (1). Reports of CRE in animals and animal settings are rare but have been documented in livestock, wildlife, and companion animals (2).

In April 2019, passive surveillance by the Veterinary Laboratory Information and Response Network of the US Food and Drug Administration identified the *bla*<sub>NDM-5</sub> gene in a carbapenem-resistant *Escherichia coli* isolated from a dog in July 2018. This isolate belonged to sequence type 167 (ST167).

A retrospective review of hospital records showed that, during July 11–August 3, 2018, seven carbapenem-resistant *E. coli* isolates were isolated from 6 animals (Table). Isolates were obtained from 5 dogs and 1 cat; all were from respiratory tract specimens, except for 2 isolates from the urine of 1 dog. All animals were housed in the intensive care unit for  $\geq 24$  hours (Appendix Figure, <https://wwwnc.cdc.gov/EID/article/26/2/19-1221-App1.pdf>). All animals overlapped with  $\geq 1$  other affected animal.

We evaluated antimicrobial use; 5/6 animals received  $\geq 4$  antimicrobial drugs before specimen submission. No animals received a carbapenem drug in the 30-day period before sample submission. A  $\beta$ -lactam was given to 5/6 animals, azithromycin to 5/6 animals, metronidazole to 4/6 animals, and enrofloxacin to 4/6 animals (Table).

The first isolate, *E. coli* 24213-18, was sequenced by using a Pacific Biosciences Sequel Sequencer (<https://www.pacb.com>) and uploaded to GenBank (BioSample SAMN11230749). This testing confirmed *E. coli* ST167 and identified a circular IncFII plasmid of 139,547 bp, which contained the *bla*<sub>NDM-5</sub> gene and additional resistance genes: *tet(A)*, *aac(6')-Ib-cr*, *aadA5*, *aadA2*, *bla*<sub>OXA-1'</sub>, *bla*<sub>CTX-M-15'</sub>, *catB3*, *dfrA17*, *dfrA12*, *sul1* (2 copies), and *mph(A)* (3).

Whole-genome sequencing was performed on all 7 isolates (24213-18, 24920-18, 27025-1-18, 27025-2-18, 27241-18, 27609-18, and 27614-18) by using the Illumina MiSeq platform (<https://www.illumina.com>). We identified antimicrobial resistance genes by using the National Center for Biotechnology Information Pathogen Detection Isolates Browser, which uses AMRFinder (<https://www.ncbi.nlm.nih.gov/pathogens/antimicrobial-resistance/AMRFinder>). The following genes were found in all 7 isolates: *aac 3-IId*, *aac(6')-Ib-cr5*, *aadA2*, *aadA22*, *aadA5*, *bla*<sub>CTX-M-15'</sub>, *bla*<sub>NDM-5'</sub>, *bla*<sub>OXA-1'</sub>, *bla*<sub>TEM-1</sub>, *ble*, *catB3*, *dfrA12*, *dfrA17*, *mph(A)*, *qacEdelta1*, *sul1*, and *tet(A)*. The *floR* gene was detected in all isolates except 27025-1-18. PlasmidFinder (<https://cge.cbs.dtu.dk/services/PlasmidFinder>) analysis confirmed the presence of an IncFII plasmid in all isolates.

NDM-5-producing *E. coli* have been reported in dogs from Finland, South Korea, and Algeria (3–5). The isolates from Finland were also ST167; the isolates from South Korea and Algeria were obtained from canine feces and identified as ST410 and ST1284. ST1284 is a double-locus variant of ST167, which suggests possible distant relatedness of these isolates; ST410 does not share any multilocus sequence type alleles with ST167 (5). In 2011, the NDM-5 carbapenemase was

**Table.** Clinical characteristics of New Delhi metallo- $\beta$ -lactamase-5–producing *Escherichia coli* isolates from 6 companion animals, United States, 2018\*

Isolate ID	BioSample accession no.	Source	Species	Breed	Age, y/sex	Concurrent diagnosis	Antimicrobial drugs in the past 30 days	Outcome
24213-18	SAMN11230749	Endotracheal wash	Canine	Great Dane	11/F	Megaesophagus; aspiration pneumonia	AMP, CLI, CAZ, ENR, MTZ	Discharged
24920-18	SAMN12190106	Lung tissue	Canine	Rottweiler	8/M	Pheochromocytoma; aspiration pneumonia	AMP, AZM, ENR, MTZ	Discharged
27025-18-1, 27025-18-2	SAMN12189820, SAMN12190134	Urine (cystocentesis)	Canine	Mixed breed	13/F	Atrioventricular block; acute kidney injury	AMP, AZM, CFZ, ENR, MTZ	Discharged
27241-18	SAMN12190501	Endotracheal wash	Canine	Beagle	5/M	Septic peritonitis after foreign body removal; protein-losing nephropathy; suspected pulmonary thromboembolism	AMP, AZM, FOX, PTZ, MTZ	Euthanized
27609-18	SAMN12190410	Endotracheal wash	Feline	Domestic shorthair	8/F	Asthma	AZM	Discharged
27614-18	SAMN12190436	Endotracheal wash	Canine	Standard poodle	8/F	Laryngeal paralysis; pneumonia	AZM, AMC, ENR	Discharged

\*All animals had been spayed or castrated. AMC, amoxicillin/clavulanate; AMP, ampicillin; AZM, azithromycin; CAZ, ceftazidime; CLI, clindamycin; CFZ, cefazolin; ENR, enrofloxacin; FOX, ceftiofur; ID, identification; MTZ, metronidazole; NCBI, National Center for Biotechnology Information; PTZ, piperacillin/tazobactam.

described in an isolate of *E. coli* (ST648) from a human in the United Kingdom who was previously hospitalized in Goa, India (6). In February 2018, three isolates of NDM-5–positive *E. coli* (ST43) were isolated from 2 patients in a skilled nursing facility in New York, New York (7). Spread of NDM-5–positive *E. coli* has occurred globally and included reports of ST167 in persons in Europe and Asia (8,9).

Healthcare-associated spread of this *E. coli* strain in the veterinary intensive care unit emphasizes the need to rapidly identify and characterize carbapenem-resistant isolates from animals. Methods to control the spread of CRE in veterinary medical settings have not yet been studied; these studies are needed to limit the spread of these pathogens in animal populations. Control measures in human healthcare settings include strict hand hygiene, use of personal protective equipment, and environmental decontamination (10). The risk for transmission of CRE from animals to persons is currently poorly understood.

It has been documented that *bla*<sub>NDM-5</sub> ST167, and carbapenem-resistant *E. coli* strains can infect humans and animals (4). Additional investigations are needed in the context of transmission between humans and animals. Characterization of CRE isolates from animals is needed to build a knowledge base and provide guidance for future studies because CRE will continue to emerge in veterinary medical settings. CRE will be a major challenge across all health fields as these organisms become more prevalent in the community. A One Health approach to antimicrobial resistance surveillance, infection prevention, and

antimicrobial stewardship could limit the spread and potential global dominance of CRE.

This study was supported in part by grant FOA PAR-17-141 and performed in collaboration with the US Food and Drug Administration Veterinary Laboratory Investigation and Response Network (FDA Vet-LIRN) under grant 1 U18 FD006669-01. PacBio sequencing of isolate 24213-18 was supported by the US Food and Drug Administration as part of routine work.

### About the Author

Dr. Cole is a veterinary microbiologist and a lecturer at the University of Pennsylvania School of Veterinary Medicine, Philadelphia, PA. His research interests include infectious diseases of dogs and cats and antimicrobial stewardship educational strategies in veterinary medicine.

### References

- Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant *Enterobacteriaceae*: epidemiology and prevention. *Clin Infect Dis*. 2011;53:60–7. <https://doi.org/10.1093/cid/cir202>
- Köck R, Daniels-Haardt I, Becker K, Mellmann A, Friedrich AW, Mevius D, et al. Carbapenem-resistant *Enterobacteriaceae* in wildlife, food-producing, and companion animals: a systematic review. *Clin Microbiol Infect*. 2018;24:1241–50. <https://doi.org/10.1016/j.cmi.2018.04.004>
- Tyson GH, Li C, Ceric O, Reimschuessel R, Cole S, Peak L, et al. Complete genome sequence of a carbapenem-resistant canine *Escherichia coli* isolate with *bla*<sub>NDM-5</sub> from a dog in the United States. *Microbiol Resour Annu*. 2019;8:e00872–19. <https://doi.org/10.1128/MRA.00872-19>
- Grönthal T, Österblad M, Eklund M, Jalava J, Nykäsenoja S, Pekkanen K, et al. Sharing more than friendship: transmission of NDM-5 ST167 and CTX-M-9 ST69 *Escherichia coli* between dogs and humans in a family, Finland, 2015.

- Euro Surveill. 2018;23. <https://doi.org/10.2807/1560-7917.ES.2018.23.27.1700497>
5. Hong JS, Song W, Park HM, Oh JY, Chae JC, Han JI, et al. First detection of New Delhi metallo- $\beta$ -lactamase-5-producing *Escherichia coli* from companion animals in Korea. *Microb Drug Resist.* 2019;25:344–9. <https://doi.org/10.1089/mdr.2018.0237>
  6. Yousfi M, Mairi A, Bakour S, Touati A, Hassissen L, Hadjadj L, et al. First report of NDM-5-producing *Escherichia coli* ST1284 isolated from dog in Bejaia, Algeria. *New Microbes New Infect.* 2015;8:17–8. <https://doi.org/10.1016/j.nmni.2015.09.002>
  7. Hornsey M, Phee L, Wareham DW. A novel variant, NDM-5, of the New Delhi metallo- $\beta$ -lactamase in a multidrug-resistant *Escherichia coli* ST648 isolate recovered from a patient in the United Kingdom. *Antimicrob Agents Chemother.* 2011;55:5952–4. <https://doi.org/10.1128/AAC.05108-11>
  8. Iregui A, Ha K, Meleny K, Landman D, Quale J. Carbapenemases in New York City: the continued decline of KPC, but new emerging threats. *J Antimicrob Chemother.* 2018;73:2997–3000. <https://doi.org/10.1093/jac/dky322>
  9. Giufrè M, Errico G, Accogli M, Monaco M, Villa L, Distasi MA, et al. Emergence of NDM-5-producing *Escherichia coli* sequence type 167 clone in Italy. *Int J Antimicrob Agents.* 2018;52:76–81. <https://doi.org/10.1016/j.ijantimicag.2018.02.020>
  10. Zong Z, Fenn S, Connor C, Feng Y, McNally A. Complete genomic characterization of two *Escherichia coli* lineages responsible for a cluster of carbapenem-resistant infections in a Chinese hospital. *J Antimicrob Chemother.* 2018;73:2340–6. <https://doi.org/10.1093/jac/dky210>

Address for correspondence: Shelley C. Rankin, University of Pennsylvania School of Veterinary Medicine, 3900 Delancey St, Philadelphia, PA 19104, USA; email: [srankin@vet.upenn.edu](mailto:srankin@vet.upenn.edu)

## Hantavirus Infection with Renal Failure and Proteinuria, Colorado, USA, 2019

Swati Chand,<sup>1</sup> Sangharsha Thapa,<sup>1</sup> Shelley Kon, Steven C. Johnson, Eric M. Poeschla, Carlos Franco-Paredes, Alfonso J. Rodríguez-Morales, Salim Mattar, Andrés F. Henao-Martínez

Author affiliations: Kathmandu University School of Medical Sciences, Kathmandu, Nepal (S. Chand, S. Thapa); University of Colorado School of Medicine, Aurora, Colorado, USA (S. Kon, S.C. Johnson, E.M. Poeschla, C. Franco-Paredes,

A.F. Henao-Martínez); Hospital Infantil de México Federico Gómez, Mexico City, Mexico (C. Franco-Paredes); Universidad Tecnológica de Pereira, Pereira, Colombia (A.J. Rodríguez-Morales); Universidad de Córdoba, Montería, Colombia (S. Mattar)

DOI: <https://doi.org/10.3201/eid2602.191349>

In North America, hantaviruses commonly cause hantavirus pulmonary syndrome (HPS). Clinical descriptions of hantavirus-associated renal disease in the Americas are scarce. Herein, we discuss the case of a 61-year-old man whose predominant manifestations were acute kidney injury and proteinuria. Clinical recognition of renal signs in hantavirus infections can reduce risk for death.

In the United States, 20–40 hantavirus cases are reported annually. Human infections result from inhalation of aerosolized secretions of infected rodents. Hantavirus pulmonary syndrome (HPS) is associated with pneumonitis and has a broad clinical spectrum that ranges from mild or no symptoms to fulminant respiratory failure. Hemorrhagic fever with renal syndrome (HFRS) is a characteristic clinical entity that manifests with fever, hypotension, and renal failure (1) and can also manifest as a mild glomerulonephritis and renal insufficiency (2). Eurasian hantaviruses (Hantaan virus, Puumala virus, and Seoul virus [SEOV]) cause HFRS; SEOV has a worldwide distribution (1). However, HPS is the clinical manifestation of most domestically acquired hantavirus infections in the United States.

HFRS in the United States was first reported in 2008 in a 22-year-old man with SEOV infection (2). Investigating a SEOV outbreak in 2017, the Centers for Disease Control and Prevention described 17 human cases in 11 states, including Colorado (3). Of these 17 patients, 9 were asymptomatic, 8 became ill, and 3 were hospitalized and recovered. The index case-patient was an 18-year-old woman with hematuria and mildly elevated creatinine who owned a pet rat (4). Published descriptions of hantavirus infection with renal manifestations in the United States are few, and the clinical characteristics of the renal injury are not often described.

We report a 61-year-old man with predominant renal manifestations of hantavirus who acquired the virus in Colorado, USA, apparently after exposure to aerosolized rodent droppings. He lived on a farm in northeastern Colorado and had cleaned his garage of extensive mouse and rat droppings 2 weeks earlier. He did not wear a mask to clean and did not own pet rats or snakes. He sought care in April 2019 for a 4-day history of fever up to 38.3°C, headache, fatigue, and myalgia. He also reported abdominal pain, anorexia, neck stiffness, and photophobia.

<sup>1</sup>These authors contributed equally to this article.

# New Delhi Metallo- $\beta$ -Lactamase-5–Producing *Escherichia coli* in Companion Animals, United States

## Appendix

Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
24213-18	A	X	X	X	X	X	X	X	X*	X	X	X	X	X	D				O						O								
24920-18	A	X	X	X	X	X	X	X	X	X	X*	X	X	X	H	D																	
27025-18														A	X	X	X	X	X	X	D		O						O*				
27241-18																					A	X	X	X	X	H	D		A	X*	D		
27609-18														A	X	X	X	X	X	D						O						O	O*
27614-18																														A	X	H*	

**Appendix Figure.** Time line characteristics of 6 companion animals infected with New Delhi metallo- $\beta$ -lactamase-5–producing *Escherichia coli*, United States, 2018. A, admitted to hospital; D, discharged from hospital; H, hospitalized but not in intensive care unit; O, outpatient visit; X, hospitalized in intensive care unit; \*, culture submission date.