Circulation of Enterovirus D68 during Period of Increased Influenza-Like Illness, Maryland, USA, 2021

Amary Fall, Nicholas Gallagher, C. Paul Morris, Julie M. Norton, Andrew Pekosz, Eili Klein, Heba H. Mostafa

Author affiliations: Johns Hopkins School of Medicine, Baltimore, Maryland, USA (A. Fall, N. Gallagher, C.P. Morris, J.M. Norton, A. Pekosz, E. Klein, H.H. Mostafa); National Institute of Allergy and Infectious Disease, National Institutes of Health, Bethesda, Maryland, USA (C.P. Morris); Johns Hopkins Bloomberg School of Public Health, Baltimore (A. Pekosz); Center for Disease Dynamics, Economics, and Policy, Washington, DC, USA (E. Klein)

DOI: https://doi.org/10.3201/eid2807.212603

We report enterovirus D68 circulation in Maryland, USA, during September–October 2021, which was associated with a spike in influenza-like illness. The characterized enterovirus D68 genomes clustered within the B3 subclade that circulated in 2018 in Europe and the United States.

In early July 2021, the United States began to relax COVID-19 infection control measures. As the number of COVID-19 cases began to fall, cases of influenza-like illness (Appendix Table 1, https://wwwnc.cdc.gov/EID/article/28/7-212603-App1.pdf) continued to be seen in the Johns Hopkins Hospital system (Baltimore, MD, USA) through October 2021 (Appendix Figure 1). Enterovirus/rhinovirus were detectable throughout the pandemic (1,2), but their positivity markedly increased to reach 20.7% (of all samples tested for enterovirus/rhinovirus) in October 2021, surpassing all other respiratory viruses (Appendix Figure 2) (2).

Enterovirus-D68 (EV-D68) was associated with a large outbreak of respiratory disease in children in North America in 2014 and was subsequently linked to the occurrence of acute flaccid myelitis (AFM) (3). After the 2014 outbreak, active surveillance of EV-D68 was implemented in many countries in Asia, Europe, Africa, and the Americas. Data obtained through surveillance during 2014–2018 suggested a biennial circulation cycle in Europe and North America (4,5). However, despite this expected biennial pattern, EV-D68 detection in 2020 was lower than anticipated, and limited cases were detected in the United States (6). This change in the circulation of EV-D68 in 2020 might have been secondary to the widespread mitigation measures for COVID-19. Of note, a recent study from 8 countries in Europe reported a rapid increase in EV-D68 infections during July 31–October 14, 2021, which coincided with a period of relaxed COVID-19 mitigation measures (7).

For this study, we collected samples positive for enterovirus/rhinovirus after the standard-of-care diagnosis at the Johns Hopkins Medical Microbiology Laboratory during September–October 2021 (Figure; Appendix). Research was conducted under Johns Hopkins Institutional Review Board protocol IRB00221396 with a waiver of consent. Remnant nasopharyngeal clinical specimens from patients that tested positive for enterovirus/rhinovirus during September–October 2021 were retrieved for the study. Genomes were made publicly available in GenBank (accession nos. OL826825–36).

We employed an optimized typing approach by using Nanopore next-generation sequencing (NGS) to characterize the enterovirus types (September–October 2021) associated with the increase in influenza-like illness. In brief, we used primers specific for enterovirus species A–D to amplify a 4,500-nt fragment that covers the whole P1 region (about half of the genome) (8) and then performed sequencing (Appendix). Of 280 enterovirus/rhinovirus-positive samples, we collected 262 for genotyping (Figure). We detected enterovirus in 28.6% of the 63 successfully sequenced samples (18/63); 94.4% (17/18) were EV-D68 and 5.6% (1/18) were coxsackievirus A6 (CV-A6). Even though the primers used for amplification were specific for enteroviruses, rhinoviruses were characterized in 45 of the 63 samples; those rhinoviruses consisted primarily of species C (26/45), followed by A (13/45) and B (6/45).

The whole cohort of patients positive for enterovirus/rhinovirus during September–October 2021 ranged in age from <1 year to >90 years; mean age was 16.7 years and median age 5 years. The male:female ratio was 1:1. On the other hand, the median age of EV-D68-positive patients was 2 years, and the male:female ratio was 1.3 (Appendix Table 2). EV-D68 was detected in 15/168 (8.9%) pediatric specimens positive for enterovirus/rhinovirus during the study time frame. Symptoms or signs of viral or respiratory illness were reported in all pediatric patients with EV-D68 (N = 15) (Appendix Table 2), and 5 patients (33.3%) were admitted and required supplemental oxygen, admission to the intensive care unit, or both. No neurologic complications including AFM...
were observed (Appendix Table 2). Of note, no AFM cases were diagnosed at Johns Hopkins Hospital during the study time frame. Most cases of enterovirus were detected in residents of the city of Baltimore (11/17). A total of 12 EV-D68 sequences, subclade B3, had a complete 5′ half of the genome (3000–4200 bp). EV-D68 genomes clustered with strains detected in 2019 from several countries in Europe (Appendix Figure 3).

We report a predominance of EV-D68 among the circulating enteroviruses during the same period in which enterovirus/rhinovirus positivity increased in this hospital system (2). The predominance of EV-D68 in our study (27% of total enterovirus/rhinovirus-typed genomes) was higher than the 0.4% and 3.6% observed in 2019 and 2020 in the United States (6) and comparable to the 24.3% reported before the COVID-19 pandemic in 2018 (6).

The EV-D68 strains detected belong to the B3 subclade, which had not been reported from the United States since 2018 (6) but was detected in Europe in 2019 (9). That report might explain why the strains we identified are more closely related to subclade B3 from the United States than to those from Europe in 2018.

This publication was made possible by support from the Sherrilyn and Ken Fisher Center for Environmental Infectious Diseases, Division of Infectious Diseases, Johns Hopkins University School of Medicine. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the Fisher Center or Johns Hopkins University School of Medicine.

H.H.M. is supported by the HIV Prevention Trials Network sponsored by the National Institute of Allergy and Infectious Diseases. Funding was provided by the Johns Hopkins Center of Excellence in Influenza Research and Surveillance (HHSN272201400007C), National Institute on Drug Abuse, National Institute of Mental Health, and Office of AIDS Research, of the NIH, DHHS (UM1 AI068613), the NIH RADx-Tech program (3U54HL143541-02S2), National Institute of Health RADx-UP initiative (grant R01 DA045556-04S1), Centers for Disease Control (contract 75D30121C11061), the Johns Hopkins University President’s Fund Research Response, the Johns Hopkins Department of Pathology, and the Maryland Department of Health. E.K. was supported by Centers for Disease Control and Prevention MnD-Healthcare Program (Grant no. U01CK000589).
About the Author
Dr. Fall is a postdoctoral research fellow in the Department of Pathology, Division of Medical Microbiology, Johns Hopkins School of Medicine. His primary research focus is respiratory viral surveillance, particularly enteroviruses and adenoviruses. Dr. Mostafa is an assistant professor of pathology and director of the Molecular Virology Laboratory at Johns Hopkins School of Medicine. Her research focuses on viral genomic evolution and its association with outbreaks and severe disease.

References

Genomic Evidence of In-Flight SARS-CoV-2 Transmission, India to Australia, April 2021

Freya Hogarth, Pasqualina Coffey, Laura Goddard, Sarah Lewis, Shereen Labib, Mathilda Wilmot, Patiyen Andersson, Norelle Sherry, Torsten Seemann, Benjamin P. Howden, Kevin Freeman, Robert Baird, Ian Hosegood, Kathleen Mc Dermott, Nick Walsh, Ben Polkinghorne, Catherine Marshall, Jane Davies, Vicki Krause, Ella M. Meumann

Author affiliations: Australian Government Department of Health, Canberra, Australian Capital Territory, Australia (F. Hogarth); The Australian National University, Canberra (F. Hogarth, B. Polkinghorne); Centre for Disease Control, Darwin, Northern Territory, Australia (P. Coffey, L. Goddard, S. Lewis, S. Labib, V. Krause); The University of Melbourne at The Peter Doherty Institute for Infection and Immunity, Melbourne, Victoria, Australia (M. Wilmot, P. Andersson, N. Sherry, T. Seemann, B.P. Howden); Royal Darwin Hospital, Darwin (K. Freeman, R. Baird, C. Marshall, J. Davies, E.M. Meumann); Qantas Airways Limited, Mascot, New South Wales, Australia (I. Hosegood); National Critical Care and Trauma Response Centre, Darwin (K. McDermott, N. Walsh); Menzies School of Health Research and Charles Darwin University, Darwin (J. Davies, E.M. Meumann)

DOI: https://doi.org/10.3201/eid2807.212466

Epidemiologic and genomic investigation of SARS-CoV-2 infections associated with 2 repatriation flights from Australia to India in April 2021 indicated that 4 passengers transmitted SARS-CoV-2 to >11 other passengers. Results suggest transmission despite mandatory mask use and predeparture testing. For subsequent flights, predeparture quarantine and expanded predeparture testing were implemented.

During the first epidemic wave of SARS-CoV-2, Australia closed its borders; during March 28, 2020–November 1, 2021, international arriving passengers were required to undergo mandatory supervised quarantine (1). This initial response contributed to the end of the first pandemic wave in June 2020 and resulted in periods of COVID-19 control throughout the country (2).

Beginning October 23, 2020, a quarantine facility in Darwin, Northern Territory, Australia, received persons who arrived via government-assisted repatriation flights. On April 15 and 17, 2021, two repatriation flights (flights 1 and 2) carrying pas-