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*CORRESPONDENCE Kimberley S. M. Benschop Kim.benschop@rivm.nl

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Editorial: Enterovirus surveillance in Europe and beyond

Kimberley S. M. Benschop^{1*}, Caroline Klint Johannesen², Sofie E. Midgley^{3,4}, Heli Harvala ^{5,6,7} and Thea K. Fischer^{2,7}

¹Centre for Infectious Disease Research, Diagnostics and Laboratory Surveillance (IDS), Centre for Infectious Disease Control (Clb), Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands, ²Department of Clinical Research, Nordsjællands Hospital, Hillerød, Denmark, ³Virus & Microbiological Special Diagnostics, Statens Serum Institut, Copenhagen, Denmark, ⁴The Danish WHO National Reference Laboratory for Poliovirus, Virus & Microbiological Special Diagnostics, Statens Serum Institut, Copenhagen, Denmark, ⁵Microbiology Services, National Health Service (NHS) Blood and Transplant, London, United Kingdom, ⁶Division of Infection and Immunity, University College London, London, United Kingdom, ⁷Department of Public Health, University of Copenhagen, Copenhagen, Denmark

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Editorial on the Research Topic Enterovirus surveillance in Europe and beyond

Enteroviruses (EV) are ubiquitous. Most infections are mild. However severe and even fatal infections occur, in particular among young children. This Research Topic on *"Enterovirus Surveillance in Europe and Beyond*" entails five research articles on EV circulation in Europe over a prolonged period including the COVID-19 pandemic years of 2020-2021. The studies describe both the epidemiological and clinical characteristics of EV infections, where two studies specifically focus on EV-D68 circulation (Uršič et al., Landaas et al.) and a fatal infection of EV-A71 (Nieminem et al.).

Increased circulation of EVs is often seen in the summer and autumn months, though the dominant EV type varies between years. The emergence of EV-D68 and its increased detection among patients with respiratory infection and acute flaccid myelitis has been noted since 2010 (1, 2). For almost a decade, circulation of EV-D68 was limited to a biennial seasonal pattern from late summer to early winter (1, 3) but since 2020, this seasonal pattern has been observed every year (4).

However, while these patterns may reflect an overall picture of EV circulation dynamics, country and regional based differences need to be accounted for as well, and in particular, the dominating types per region/country and even per reporting institute seem to vary.

The study by Johannesen et al. on EV infections linked to hospitalizations and outpatient visits in Denmark 2015-2022, shows that while the COVID-19 pandemic led to a drastic decrease in number of cases reported, it has not affected the seasonal patterns (also seen by Uršič et al., Landaas et al. and Dudman et al. Central nervous system (CNS) infections were commonly found among neonates in hospitalized settings, while skin infections were more common among outpatients. The age distribution of patients with CNS infection and skin infections remained similar before and after the pandemic, with neonates commonly affected with CNS infections and children aged 1-2 years with skin

infections respectively. Of interest is that Dudman et al. who studied EV infections from 2016-2022 noted an increase in detection skin infections with coxsackievirus A6 (CVA6), a virus most often associated with skin infections and in particular atypical hand foot and mouth disease. The dominance of CVA6 continued also after the COVID-19 pandemic.

In a similar study period, Uršič et al. showed a similar seasonal pattern of EV circulation for 2014 and 2016. In addition, they demonstrated EV-D68 circulation in Slovenia during the biannual years pre COVID-19 pandemic, 2014-2016, and hardly any cases after that. Landaas et al. also showed an upsurge of EV-D68 cases in these two years in Norway when studying a period from 2012-2022, with low numbers in 2018, 2019 and 2021.

Of interest is that for 2021, a European wide upsurge of EV-D68 was observed following ease of the COVID-19 pandemic restriction (4) among 58 institutes in 19 European countries participating in the European Non Polio enterovirus network (ENPEN). Simões et al. indeed stated that large differences in the proportions of EV-D68-positive samples were observed among countries/reporting institutes. While most infections in the 2021 study by Simões et al. were identified among children <5 years of age, Landaas et al. and Uršič et al. both showed that the pediatric population of Norway and Slovenia deviated from the European wide upsurge in 2021, with hardly any cases being reported. In contrast, Landaas et al. reports a large EV-D68 outbreak in 2022 in the pediatric Norwegian population, yet only two cases were reported by Dudman et al. in Oslo, Norway, despite screening all age groups. The 2022 EV-D68 upsurge was previously not seen by other countries (Sten et al. manuscript in preparation) and also not seen in Slovenia (Uršič et al.).

The studies in this Research Topic show the differences in the epidemiology of EV infections between countries/institutes. This may reflect the true circulation in these countries although its more likely to reflect the lack of standardized public health surveillance guidelines and/or systems, challenging the comparability among these and other studies (4-7). These include the lack of a uniform case definition and sampling strategy, and differences in screening and typing methods across institutes. In addition, while the European region has set up uniform legal and ethical regulations concerning data sharing, the implementation and interpretation proves to be limiting uniform data sharing. The varied and in some cases incomplete reporting to larger ENPEN studies may lead to biases in the data. As such to understand and better determine the disease burden of EV infection, we need clear standardization of data collection with comprehensive reporting. Utilizing existing surveillance systems for poliovirus and non-polio enteroviruses, enables synergy between the different surveillance systems (clinical, sewage and AFP surveillance) which is needed for overall enterovirus surveillance as for poliovirus surveillance specifically (Fischer et al., manuscript submitted). The final study in this Research Topic reflects on the identification of a fatal case of EV-A71 in 2019. Despite their effort in enhanced communication, surveillance, and typing the overall number of clinical EV positive cases was low in 2019, yet environmental surveillance showed continued circulation of EVs and the EV-A71 strain.

ENPEN is an interdisciplinary consortium which brings together specialists from clinical, diagnostic and research areas including clinical and molecular virology, epidemiology, public health, neurology, and pediatric infectious diseases across Europe and beyond. The main aim of ENPEN is to ensure harmonized, coordinated and standardized (real-time) data sharing and collaborative research.

Author contributions

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Conflict of interest

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