European surveillance for enterovirus D68 during the emerging North-American outbreak in 2014.

Poelman R1, Schuffenecker I2, Van Leer-Buter C3, Josset L4, Niesters HG3, Lina B4; ESCV-ECDC EV-D68 study group.

1The University of Groningen, University Medical Center Groningen, Department of Medical Microbiology, Division of Clinical Virology, Groningen, The Netherlands. Electronic address: r.poelman@umcg.nl.
2National Enterovirus Reference Centre, Laboratoire de Virologie, Centre de Biologie Est des Hospices Civils de Lyon, Bron, France.
3The University of Groningen, University Medical Center Groningen, Department of Medical Microbiology, Division of Clinical Virology, Groningen, The Netherlands.
4National Enterovirus Reference Centre, Laboratoire de Virologie, Centre de Biologie Est des Hospices Civils de Lyon, Bron, France; Virpath Lab, EA4610, Faculté de Médecine Lyon Est, Université Claude Bernard Lyon1, Université de Lyon, Lyon, France.

ABSTRACT
BACKGROUND: In August and September 2014, unexpected clusters of enterovirus-D68 (EV-D68) infections associated with severe respiratory disease emerged from North-America. In September, the European Centre for Disease Prevention and Control (ECDC) asked European countries to strengthen respiratory sample screening for enterovirus detection and typing in cases with severe respiratory presentations.

OBJECTIVES: To provide a detailed picture of EV-D68 epidemiology in Europe by conducting a retrospective and prospective laboratory analysis of clinical specimens.

STUDY DESIGN: An initiative supported by the European Society for Clinical Virology (ESCV) and ECDC was launched to screen for EV-D68 in respiratory specimens between July 1st and December 1st 2014 in Europe and to sequence the VP1 region of detected viruses for phylogenetic analytic purposes.

RESULTS: Forty-two institutes, representing 51 laboratories from 17 European countries, analyzed 17,248 specimens yielding 389 EV-D68 positive samples (2.26%) in 14 countries. The proportion of positive samples ranged between 0 and 25% per country. These infections resulted primarily in mild respiratory disease, mainly detected in young children presenting with wheezing and in immuno-compromised adults. The viruses detected in Europe are genetically very similar to those of the North-American epidemic and the majority (83%) could be assigned to clade B. Except for 3 acute flaccid paralysis (AFP) cases, one death and limited ICU admissions, no severe cases were reported.

CONCLUSIONS: The European study showed that EV-D68 circulated in Europe during summer and fall of 2014 with a moderate disease burden and different pathogenic profile compared to the North-American epidemic.
The emergence of enterovirus D68 in a Dutch University Medical Center and the necessity for routinely screening for respiratory viruses.

Poelman R\(^1\), Schölvinck EH\(^2\), Borger R\(^3\), Niesters HG\(^1\), van Leer-Buter C\(^3\).

\(^1\)Department of Medical Microbiology, Division of Clinical Virology, University Medical Center Groningen, Groningen, The Netherlands.

\(^2\)Beatrix Children's Hospital, The University of Groningen, University Medical Center Groningen, Groningen, The Netherlands.

\(^3\)Department of Medical Microbiology, Division of Clinical Virology, University Medical Center Groningen, Groningen, The Netherlands. Electronic address: c.van.leer@umcg.nl.

ABSTRACT

BACKGROUND: Since August 2014, an increase in infections caused by enterovirus D68 (EV-D68) was reported in the USA and Canada, for the most part in children presenting with severe respiratory symptoms.

OBJECTIVES: To determine whether an increase in severe EV-D68 respiratory infections was observed in our region.

STUDY DESIGN: Samples from patients with respiratory symptoms were screened for viral pathogens, including rhinovirus and enterovirus. Subsequently, samples positive for rhinovirus and enterovirus were routinely sequenced for phylogenetic analysis. Furthermore, an additional method was used to detect EV-D68 specifically.

RESULTS: During the first three quarters of the year 2014, 1896 respiratory samples were analyzed; 39 (2\%) of them tested positive for enterovirus. Eighteen samples tested positive for EV-D68, obtained from 16 different patients admitted to our hospital. Eleven were children below the age of 18, of whom five children needed intensive care treatment. The remaining five samples were from adults, who all had an underlying disease; three were transplant patients (heart, lung and renal transplantation), the other two had an underlying lung condition (COPD, asthma). Phylogenetic analysis showed a close relationship with the strains circulating currently in the USA, all belonging to the known EV-D68 genetic subtypes.

CONCLUSIONS: We observed an increase of EV-D68 infections in our population, both in children as well as in adult. In 2014 there have been 16 cases so far, compared to none in 2011 and 2013 and a single case in 2012. Phylogenetic analysis identified two similar clusters as shown in the USA and Canada.
Severe enterovirus 68 respiratory illness in children requiring intensive care management.
1Division of Infectious Diseases, Children's Mercy Hospital, Kansas City, MO, USA. Electronic address: jeschuster@cmh.edu.
2Division of Critical Care, Children's Mercy Hospital, Kansas City, MO, USA.
3Division of Pathology and Laboratory Medicine, Children's Mercy Hospital, Kansas City, MO, USA.
4Division of Infectious Diseases, Children's Mercy Hospital, Kansas City, MO, USA.
5Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, GA, USA.

ABSTRACT
BACKGROUND:
Enterovirus 68 (EV-D68) causes acute respiratory tract illness in epidemic cycles, most recently in Fall 2014, but clinical characteristics of severe disease are not well reported.

OBJECTIVES:
Children with EV-D68 severe respiratory disease requiring pediatric intensive care unit (PICU) management were compared with children with severe respiratory disease from other enteroviruses/rhinoviruses.

STUDY DESIGN:
A retrospective review was performed of all children admitted to Children's Mercy Hospital PICU from August 1-September 15, 2014 with positive PCR testing for enterovirus/rhinovirus. Specimens were subsequently tested for the presence of EV-D68. We evaluated baseline characteristics, symptomatology, lab values, therapeutics, and outcomes of children with EV-D68 viral infection compared with enterovirus/rhinovirus-positive, EV-D68-negative children.

RESULTS:
A total of 86 children with positive enterovirus/rhinovirus testing associated with respiratory symptoms were admitted to the PICU. Children with EV-D68 were older than their EV-D68-negative counterparts (7.1 vs. 3.5 years, P=0.01). They were more likely to have a history of asthma or recurrent wheeze (68% vs. 42%, P=0.03) and to present with cough (90% vs. 63%, P=0.009). EV-D68 children were significantly more likely to receive albuterol (95% vs. 79%, P=0.04), magnesium (75% vs. 42%, P=0.004), and aminophylline (25% vs. 4%, P=0.03). Other adjunctive medications used in EV-D68 children included corticosteroids, epinephrine, and heliox; 44% of EV-D68-positive children required non-invasive ventilatory support.

CONCLUSIONS:
EV-D68 causes severe disease in the pediatric population, particularly in children with asthma and recurrent wheeze; children may require multiple adjunctive respiratory therapies.