RAPID RISK ASSESSMENT

Enterovirus 68 detected in the USA and Canada

First update, 15 October 2014

Main conclusions

Since mid-August 2014 and as of 13 October 2014, local health authorities in 46 States and the District of Columbia in the US have notified the US Centers for Disease Control and Prevention (CDC) of 691 laboratory-confirmed enterovirus 68 (EV-D68) infections. Some regions in Canada have also been detecting respiratory illness associated with EV-D68 infection since September 2014 and, as of 6 October 2014, 75 cases of EV-D68 had been confirmed by the National Microbiology Laboratory at the Public Health Agency of Canada (PHAC). Following two scientific reports detailing clusters of neurological illness including acute flaccid paralysis cases (AFP), media in the USA have reported several small clusters of neurological illness potentially associated with EV-D68 infection. Moreover, Canada has reported a small number of children with some paralysis who also have EV-D68 infection.

- As yet, an epidemiological link has not been established between the EV-D68 and the neurological illness clusters reported in several States across the US, and it cannot be ruled out that the virus is circulating independently at several locations.
- To date, EU/EEA countries have not reported growing numbers of acute respiratory infections or an increase in hospital admissions.
- To date, European AFP surveillance has not detected unusual clusters or unexpected trends.
- Sporadic cases of EV-D68 have been documented in several EU/EEA countries in recent years. In 2014, EV-D68 was detected in at least four EU/EEA countries but no epidemic clusters of severe disease have been reported and none of the Member States have so far issued an Early Warning and Response System (EWRS) notification.
- The likelihood of cases being laboratory-confirmed in EU/EEA countries is low because most countries do not routinely screen for EV-D68, and the disease is not notifiable.
- In cases of severe respiratory disease, if all other respiratory pathogen detections are negative, or if rhino-/enterovirus is detected initially, EV-D68 should be considered as the causative pathogen of the disease. More systematic testing of severe respiratory illness cases for EV-D68 could be considered in EU/EEA countries to better document the incidence of disease associated with this virus.
- EU/EEA countries need to remain vigilant and consider strengthening respiratory sample screening for enteroviruses and enterovirus typing.
- EU/EEA countries should consider improving the quality of their AFP surveillance in order to enhance polio surveillance and detect unusual clusters or trends among non-polio AFP cases. AFP cases should be tested for polio and other enteroviruses.
- Based on information currently available to ECDC, the risk of EV-D68 transmission in EU/EEA countries is moderate because the circulation of this strain in the population seems to be low.

Suggested citation: European Centre for Disease Prevention and Control. Enterovirus D68 detections in the USA and Canada – First update 15 October 2014. Stockholm: ECDC; 2014.

Source and date of request

ECDC internal decision, 6 October 2014.

Public health issue

This update of the rapid risk assessment of severe respiratory illness caused by enterovirus 68 (EV-D68) and possibly associated acute flaccid paralysis (AFP) cases in the USA and Canada addresses the following public health questions:

- Has the risk to EU citizens from the transmission of enterovirus 68 (EV-D68) in the USA and Canada changed since the rapid risk assessment of 21 August 2014, considering the updated epidemiological information?
- What is the risk to the EU population posed by the detection of clusters of non-polio AFP cases in USA and reports in Canada of a small number of children with neurological symptoms and EV-D68 infection?
- Should the EU Member States increase their preparedness for the detection of this virus, in particular the laboratory capacity to detect it in the EU, and sensitise AFP surveillance?

Previous rapid risk assessments

ECDC has published a rapid risk assessment on severe respiratory illness caused by enterovirus 68 (EV-D68) in the USA and Canada [1].

Consulted experts

ECDC internal response team involved in the production of the risk assessment: Eeva Broberg, Josep Jansa, Kaja Kaasik-Aaslav, Laurence Marrama, Niklas Danielsson, Pasi Penttinen, Marc Struelens.

External reviewers
Tom Wong, Teresa Mersereau and Francesca Reyes Domingo, Public Health Agency, Canada.
Sergei Deshevoi, WHO Regional Office for Europe.

Event background information

Current epidemiological situation in the USA

From mid-August to 13 October 2014, 691 people from 46 States and the District of Columbia were diagnosed with respiratory illness caused by EV-D68. The cases of EV-D68 infection were confirmed by the Centers for Disease Control and Prevention (CDC) or state public health laboratories, which then notified CDC. This represents an increase in the number of confirmed and suspected cases associated with this virus in comparison with reports from previous years. During the period 2009–2013, the CDC's National Enterovirus Surveillance System (NESS) received only 79 reports of EV-D68. Small clusters were also reported in 2009–2010 [2].

The 46 States that reported cases are: Alabama, Arkansas, California, Colorado, Connecticut, Delaware, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, Nebraska, New Hampshire, New Jersey, New Mexico, New York, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.

The first signal for this event was recorded on 30 August 2014 and confirmed on 8 September 2014 when CDC reported that:

- on 19 August 2014, a paediatric hospital in Kansas City (Missouri) notified CDC of an increase in patients admitted with severe respiratory illness compared to historical data. In addition, an increase in detections of rhino-/enterovirus by PCR in nasopharyngeal specimens was reported, starting on 5 August 2014;
- on 23 August, a paediatric hospital in Chicago (Illinois) notified CDC of an increase in patients with similar symptoms to those in Kansas City. This was also confirmed by the Illinois Department of Public Health.

According to the US CDC, this year, almost all the confirmed cases of EV-D68 infection have been among children. Many of the children had asthma or a history of wheezing. Five deaths have been associated with EV-D68 infection and for one of the fatal cases, EV-D68 was the only pathogen detected. For another case, EV-D68 was detected together with *Staphylococcus aureus* sepsis. The role played by EV-D68 infection in these deaths is unclear at this time and state and local health departments are continuing to investigate.

CDC provides regular updates on the number of cases and the States reporting confirmed EV-D68 infections.

On 3 October 2014, two reports were published on clusters of neurological illness, including acute flaccid paralysis (AFP) possibly associated with EV-D68 [3,4]:

- Between 8 August and 15 September 2014, nine children evaluated at one hospital in Colorado had developed symptoms of neurological illness within two weeks of a febrile and in most cases acute respiratory illness. The illness was characterised by extreme weakness, cranial nerve dysfunction (e.g. diplopia, facial droop, dysphagia, or dysarthria) or both. Nasopharyngeal samples from four of these children were positive for EV-D68.
- Between January 2012 and May 2014, 23 cases of AFP, mainly children with anterior myelitis, were detected by active surveillance in California. Samples from two of these cases were positive for EV-D68.

Following these reports, media reports from USA have emerged on small clusters of AFP or various neurological syndromes associated with EV-D68 detections from several States in USA. Reports of a small number of children in Canada with symptoms of paralysis and EV-D68 infection have also been identified. These reports are under investigation by public health authorities.

Current epidemiological situation in Canada

Some regions in Canada have been detecting respiratory illness associated with EV-D68 infection since September 2014. On 15 September 2014, Alberta Health Services reported 18 cases of EV-D68 among hospitalised patients under the age of 18. Nine cases were among children admitted to a Calgary children's hospital, with a diagnosis of asthma or bronchiolitis between 1 and 11 September 2014. As of 3 October 2014, confirmed cases had also been reported in Ontario, British Columbia, Manitoba and Saskatchewan [5].

As of 3 October 2014, the provincial laboratory in British Columbia had confirmed nine sporadic cases of EV-D68 in children (aged 0–19 years: 6 < 10 years of age and three aged 10–19 years). No clusters/outbreaks or increases in severe respiratory illness cases have been detected to date and overall rates of influenza-like illness (ILI) remain within or below expected ranges for this time of year. Monitoring continues in order to detect any possible upswing in ILI activity [6].

As of 6 October 2014, 75 cases of EV-D68 have been confirmed by sequencing at PHAC's National Microbiology Laboratory, with specimen collection dates between August and September 2014. No deaths due to EV-D68 have been reported.

Epidemiological background – EV-D68 infections

Since the first isolation of EV-D68 in four children with respiratory illness in California in 1962 [7], EV-D68 infection, which is not a notifiable disease, has rarely been reported. Ten publications which reported similar symptoms during 2006–2011 in Asia, Europe and the United States were retrieved from the scientific literature [8], which also contained reports of deaths associated with EV-D68 [9]. Table 1 provides an overview of publications on EV-D68 epidemiology with regard to reports of acute respiratory illness worldwide between 2006 and 2011.

In Europe, only scarce information is available on earlier and current circulation of EV-D68. A retrospective study (1994–2010) in the Netherlands found 71 positive specimens in samples collected for surveillance of acute respiratory infections; 67 (94%) of which were from symptomatic patients [10]. Following the 2010 outbreak, no cases were detected in 2011, 10 in 2012, three in 2013, and eight in 2014 so far, all in respiratory specimens from patients with respiratory symptoms (personal communication).

Since 2008, 60 EV-D68 cases have been reported in France through the National Enterovirus Network (personal communication), 63% of which had respiratory symptoms. In 2014, one respiratory case was notified in a baby (personal communication).

In the United Kingdom, seven cases in young children were reported during 2012, three in 2013, and two in 2014. Nine of the twelve cases were diagnosed from respiratory samples (personal communication).

In Finland, several different enteroviruses have been circulating in 2014, and one EV-D68 detection has been confirmed in one diagnostic laboratory (data does not cover the whole country; personal communication).

Table 1. Overview of studies where EV-D68 has been associated with respiratory disease, 2006–2011

Date/time period	Country/region	Number of cases and/or positive samples for EV-D68	Common signs and symptoms upon presentation	Demographics	Underlying illness	Comment	Ref.
Aug–Dec 2006 and Jan–Dec 2008	China	11 in 2006; two in 2008 out of 130 human enterovirus-positive cases	Pharyngeal congestion, myalgia, headache, chills, sore throat, rhinorrhoea, sneezing, cough	Adults with acute respiratory tract infection		A large follow-up of respiratory illness in >15-year-olds over the period August 2006 through April 2010	[11]
May 2008–May 2009	Philippines (eastern Region)	21 (2.6%) out of 816 samples collected from patients hospitalised with pneumonia	Cough, difficulty breathing, wheezing and retractions	17 (81%) out of 21 were aged 0–4 years	Not specified	Two fatalities. Sampling done only among paediatric patients	[12]
Sep 2009 to Jun 2010	France (north-east)	Of the 16 HEV strains, 10 (63%) were identified as the EV-D68 genotype	Acute wheezing or bronchitis	651 consecutive paediatric patients tested. The 10 EV-D68 positive patients were aged six months to 10 years (median: 3.8 years) with a male–female of 1:1.5.	Eight out of 10 EV-D68-positive patients had underlying pathologies (not specified)	Sampling among hospitalised paediatric patients. None of the 10 EV-D68-positives required admission to ICU.	[13]
Jul–Oct 2010	Japan (reports from local public health authorities)*	>120 cases	* Asthmatic bronchitis, pneumonia, febrile convulsions (1 case)	* 10 out 11 paediatric patients were aged 0–4 years (the study did not include patients aged 20 years and over	Not specified	* Clinical and demographic information assessed in 11 paediatric patients only. One fatality (boy aged four years)	[8]
Aug–Oct 2009	Pennsylvania, USA	28 (42%) out of 66 children who tested positive for rhinovirus were EV-D68 positive	-	15 (54%) out of 28 patients who were EV-D68 positive were aged 0–4 years. No information on the age distribution of the other patients.	-	15 (54%) out of 28 admitted to ICU. No fatalities. Mean stay in hospital: five days.	[8]
Aug–Sept 2010	Arizona, USA	18 patients with respiratory illness. EV-D68 isolated in five of seven specimens sent to CDC.	Cough and tachypnea or hypoxemia, wheezing, abnormal lung examination	Not specified	Not specified	Increase in paediatric cases triggered investigation	[8]
1994–2010	The Netherlands (nationwide)	Biobank of GP surveillance for ARI: 240 (2.4%) of 9 979 specimens were EV positive and 57 (24% of all EV) were EV-D68. Children cohort study: 76 (2.7%) of 2 764 specimens were EV positive and 13 (12% of all EV) were EV-D68.	GP surveillance: EV-D68-positive patients had significantly more dyspnoea, cough, and bronchitis when compared to EV-D68-negative patients. Children cohort study: mild symptoms, cough.	GP surveillance: Highest prevalence of EV-D68-positive patients was in those aged 50–59 years. Highest prevalence of EV-D68-negative patients in those aged 10 years or under.	-	Samples collected as part of general practice sentinel ARI surveillance (1994–2010) and three child cohort studies (2004–2009). Highest number of EV-D68-positive patients in 2010 over a six-week period.	[10]
Oct 2008–Oct 2009	Italy (Pavia)	12 out of 1 500 samples collected	Adult and paediatric patients admitted with acute respiratory illness.	-	-	-	[14]
Aug–Nov 2010	The Netherlands (Groningen)	24 patients with EV-D68 out of 231 admitted with respiratory illness	Exacerbation: asthma/wheezing (10 patients), pneumonia (6), upper respiratory tract infection (8).	One month to 72 years of age (median: 14 years), 10 patients were under 10 years (42%).	A total of 14 with underlying pulmonary disease; five with unspecified underlying chronic illness	Five patients admitted to ICU. No fatalities.	[15]
2006–2011	Thailand	25 EV-D68 cases in Thai children with respiratory illnesses from 2006–2011 (n=1810)	Fever, cough, dyspnoea, and wheezing	Majority of cases were children aged >5 years (64%)		36% required hospitalisation	[16]

ECDC threat assessment for the EU

Is the increased number of cases of EV-D68 in the USA and Canada unexpected?

The trend towards increasing detections of the EV-D68 in recent years has been unexpected compared to historical data [8]. In the USA, the authorities have reported that the upsurge in severe respiratory illness cases, particularly in paediatric hospitals, has been unexpectedly high in comparison to previous years, at least in some regions. EV-D68 is not nationally notifiable in Canada. As such, the Public Health Agency of Canada cannot determine at this time whether the increase in the number of cases of EV-D68 identified since September is unexpected, since surveillance data from previous years are not available for comparison.

The change in the antigenicity and receptor properties of EV-D68, now binding to upper respiratory tract sialic acid receptors compared to the earlier lower respiratory tract binding [9], would suggest a greater adaptation for human infection and transmission between humans. However, it would not explain the more severe outcomes of the EV-D68 infection. It cannot be ruled out that the increased number of confirmed cases in 2014 in the USA and Canada are a surveillance artefact related to increased laboratory testing of acute respiratory illnesses with improved assays. Several European countries have reported EV-D68 cases for a number of years, both in hospitals and the community (Table 1). It is likely that EV-D68 is circulating in other countries as well, but has not been detected/reported due to current diagnostics.

In temperate countries, enteroviruses typically circulate with summer–autumn seasonality. In addition, the apparent severity of EV-D68 may be an artefact and relate to the fact that the severe cases are more likely to be investigated. There are only a few community-based studies assessing the incidence of EV-D68 infection in the general population.

Is the EV-D68 strain currently circulating in the USA and Canada already circulating in the EU?

Some of the EV-D68 viruses detected by the National Microbiology Laboratory of Public Health Agency of Canada were highly similar to the main clade identified in the United States, while others were similar to a few other clades also circulating in the US. EV-D68 is currently circulating in the EU/EEA Member States and has been detected in Finland, France, the Netherlands, and the United Kingdom in 2014 (personal communication). Not all characteristics of those viruses are known, but the viruses in the Dutch cluster are in the same major genetic group as the viruses currently circulating in the US (personal communication). There are, however, also viruses of a different genetic group that have been detected (personal communication). There are ongoing studies to further characterise the circulating EV-D68 viruses both in North America and in Europe. None of the Member States has so far issued an Early Warning and Response System (EWRS) notification. And no EV-D68 isolations have been reported from the WHO European Region through the polio laboratory network (personal communication).

What is the current status of non-polio enterovirus surveillance in Europe?

Respiratory infections of rhinoviruses or non-polio enteroviruses are not notifiable in the EU/EEA. Only Belgium, Romania and the Slovak Republic conduct syndromic surveillance of severe acute respiratory infections (SARI). Additionally, Finland, France, Ireland, Spain, Sweden and the United Kingdom report laboratory-confirmed influenza infections of ICU patients to the European Surveillance System (TESSy) and may possibly use the same system to report other pathogens such as EV-D68.

Only a few EU/EEA countries conduct enterovirus surveillance and ECDC does not yet have information on which countries have established surveillance schemes for respiratory specimens (screening for enteroviruses) or have other schemes in place to test for rhino-/enteroviruses (e.g. using acute respiratory infection sentinel sampling, which is part of influenza surveillance, to focus on rhino-/enteroviruses during the summer and autumn months). Information is currently being collected on national sentinel surveillance activities for monitoring influenza and other respiratory viruses as a cause of acute respiratory infection. This collection is part of the new ECDC EULabCap monitoring system of laboratory capabilities in the EU/EEA.

ECDC does not have a good overview of activities in Member States aimed specifically at the detection of non-polio enteroviruses, and it is likely that diagnostic or enhanced surveillance processes vary considerably from country to country.

Should the EU Members State increase their preparedness for the detection of this virus, in particular the laboratory capacity to detect it in the EU, and sensitise AFP surveillance?

Some diagnostic laboratories based in hospitals or the community may encounter EV-D68 in clinical samples, but they will not necessarily pass on their findings to the national reference centres for enteroviruses, thus reducing the overall awareness of EV-D68 infections. When receiving samples from patients suffering from severe respiratory symptoms, clinical and hospital laboratories should be aware that EV-D68 could be the cause of infection.

Earlier data show that some molecular detection assays, e.g. multiplex PCR assays for respiratory pathogens, may not be sensitive enough to detect EV-D68. Alternatively, the assays may falsely detect EV-D68 as a rhinovirus [17]. Therefore, it is important that the laboratories compare their primer sets (also from commercial assays) to the publically available EV-D68 sequences and make all necessary adjustments to their detection algorithms. However, even perfectly tuned algorithms and associated assays would detect EV-D68 only as an enterovirus. In order to identify enterovirus 68, sequence typing is necessary, which is usually not performed in clinical laboratories.

It is likely that individual cases of EV-D68 may remain undetected in the EU/EEA because, for example, many of the rhinovirus-positive clinical specimens would not be further characterised through sequencing. However, if a large outbreak of severe respiratory disease were to occur in any of the Member States, the causative pathogen would be characterised. National reference laboratories that are members of the European Polio Laboratory network can offer enterovirus typing in the EU/EEA countries. Furthermore, some diagnostic and public health laboratories can identify, characterise and genotype a large variety of viruses including rhino- and enteroviruses.

It is important that the laboratories which detect and type EV-D68 from clinical samples publish the genomic sequences of those viruses on open-access sequence databases, such as GenBank, to ensure that it is possible to compare with viruses from other countries.

AFP surveillance for polio is established in most, but not all, EU countries and WHO's Regional Office for Europe receives weekly case-based reports from these countries [18]. However, the quality of AFP surveillance in most EU countries is not optimal and improving the coverage and timeliness of the surveillance would benefit not only polio surveillance but also the detection of clusters or trend changes in non-polio AFPs.

Should this virus become established in the EU, are there specific groups at increased risk of infection and severe disease, and what options exist to mitigate this risk?

Based on the age profiles of earlier outbreaks, children under 10 years of age are at risk of severe EV-D68 infection, especially if they are affected by an underlying illness in the respiratory tract such as asthma. However, EV-D68 can also infect adults. It is possible that respiratory enterovirus subtypes are more pathogenic than rhinovirus strains which could lead to more severe respiratory symptoms in acute cases [13] [15].

It is important that the management of underlying respiratory illnesses of children, such as asthma, is optimised according to national and European guidelines.

Clinicians should be made aware of the current reports of EV-D68 in North America and remain vigilant for possible increases in unexpected infections causing respiratory illness, especially among children returning from North America. In general, enteroviruses circulate and peak in summer and autumn, so it is not unusual to see additional cases caused by enteroviruses at this time of year.

Enteroviruses, such as EV-D68, belong to the same category as common cold viruses and can spread from person to person through coughing and sneezing, by close contact with infected persons, or by touching a contaminated surface. Therefore it is important to remind people who are ill of the most basic hygiene measures (including hand washing, avoiding contact and staying home if sick) to control transmission.

ECDC is closely monitoring the situation and will continue to inform Member States if additional EV-68 cases are confirmed in the USA, Canada and EU/EEA Member States.

What is the risk posed by the detection of clusters of non-polio AFP cases in USA and Canada?

It is unclear whether the clusters of neurological illness and AFP represent a true increase in such cases in North America. Unlike Canada, USA does not have a surveillance system for AFP. Public health authorities are also investigating whether such clusters are causally associated with EV-D68. If there is a genuine increase in AFP or other neurological symptoms associated with an increase in community transmission of EV-D68, it is likely that such transmission and cases would also be occurring in the EU now or would begin to in the future. Countries with high-quality AFP surveillance and/or high-quality enterovirus surveillance would be able to detect such clusters or changes in trends rapidly.

According to case-based AFP reports submitted to WHO's European Region from several European countries, no unusual clusters or trends were detected during August-September 2014 (personal communication). However these reports have not been received from all countries in the Region and the quality of surveillance in the reporting countries is extremely variable.

Conclusions

- Since mid-August 2014, some regions in the USA and Canada have been experiencing an increase in reports of severe respiratory illness associated with EV-D68 infection. As of 8 October 2014, EV-D68 had been detected in 46 States across the US and five provinces in Canada.
- It remains unclear if increased testing or improved sensitivity of surveillance has contributed to the current increase in EV-D68 infections in the USA and Canada, or if a change in the pattern of the disease caused by EV-D68 is the underlying cause of the current epidemic. There is no detailed description of the clinical picture of EV-D68 cases in the USA and Canada.
- As yet, an epidemiological link has not been established between the EV-D68 and the neurological illness clusters reported in several States across the US, and it cannot be ruled out that the virus is circulating independently at several locations.
- Concomitant clusters of neurological illness, including AFP, are being detected and reported in several regions of North America, however EV-D68 is not consistently detected from patients and a causal association has not been shown.
- Patterns of transmission for EV-D68 are thought to be similar to the rhinovirus transmission, through direct and respiratory droplet transmission, with an incubation period of a few days.
- Initial contacts with several EU/EEA countries have not indicated a growing number of acute respiratory infections or an increased number of hospital admissions.
- The likelihood of cases of severe respiratory disease associated with laboratory-confirmed EV-D68 infection being detected and reported in EU/EEA countries is low because diagnostic laboratories in most countries do not routinely screen and identify EV-D68, and the disease is not notifiable.
- In cases of severe respiratory disease if all other respiratory pathogen detections are negative, or if rhino-/enterovirus is detected initially, specific testing for EV-D68 should be considered to establish the causative pathogen of the disease. More systematic testing of severe respiratory illness cases for EV-D68 could be considered in EU/EEA countries to better document the incidence of disease associated with this virus.
- Clinicians and public health authorities in EU/EEA countries need to remain vigilant and consider increasing respiratory sample screening for enteroviruses and enterovirus typing as there is an apparent upsurge in the detection of EV-D68 cases in the USA and Canada at present.
- A working group has been established in collaboration with the European Society of Clinical Virology to assess the extent of EV-D68 detections in EU/EEA countries during 2014.
- EU/EEA countries should consider improving the quality of their AFP surveillance in order to enhance polio surveillance and detect unusual clusters or trends among non-polio AFP cases.

References

1. ECDC. Enterovirus 68 detections in the USA and Canada 2014. Available at: http://ecdc.europa.eu/en/publications/Publications/enterovirus-68-USA-Canada-rapid-risk-assessment.pdf.
2. Nelson R. Outbreaks of enterovirus D68 continue across the USA. The Lancet Respiratory Medicine. (in press).
3. Centers for Disease Control and Prevention. Acute Flaccid Paralysis with Anterior Myelitis — California, June 2012–June 2014. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm63e1003a2.htm?s_cid=mm63e1003a2_w.
4. Centers for Disease Control and Prevention. Acute Neurological Illness of Unknown Etiology in Children — Colorado, August–September 2014. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm63e1003a1.htm?s_cid=mm63e1003a1_w.
5. National Collaborating Centre for Infectious Diseases. What do we know about the current and previous outbreaks of Enterovirus D68 (EV-D68)? 2014. Available at: http://www.nccid.ca/disease-debrief-ev-d68#Q1.
6. British Columbia Centre for Disease Control. Emerging Respiratory Virus Bulletin: MERS-CoV, Influenza A(H7N9) and A(H3N2)v, Enterovirus D68: Canada; 2014. Available at: http://www.bccdc.ca/NR/rdonlyres/88FD3DD4-BEB0-4F29-93C0-6093A7AFBD4B/0/Full_ERVUpdate20141004.pdf.
7. Schieble JH, Fox VL, Lennette EH. A probable new human picornavirus associated with respiratory diseases. American Journal of Epidemiology. 1967 Mar;85(2):297-310.
8. Centers for Disease Control and Prevention. Clusters of acute respiratory illness associated with human enterovirus 68--Asia, Europe, and United States, 2008-2010. MMWR Morbidity and Mortality Weekly Report. 2011 Sep 30;60(38):1301-4.
9. Imamura T, Okamoto M, Nakakita S, Suzuki A, Saito M, Tamaki R, et al. Antigenic and receptor binding properties of enterovirus 68. Journal of Virology. 2014 Mar;88(5):2374-84.
10. Meijer A, van der Sanden S, Snijders BE, Jaramillo-Gutierrez G, Bont L, van der Ent CK, et al. Emergence and epidemic occurrence of enterovirus 68 respiratory infections in the Netherlands in 2010. Virology. 2012 Feb 5;423(1):49-57.
11. Xiang Z, Gonzalez R, Wang Z, Ren L, Xiao Y, Li J, et al. Coxsackievirus A21, enterovirus 68, and acute respiratory tract infection, China. Emerg Infect Dis. 2012 May;18(5):821-4.
12. Imamura T FN, Suzuki A et al. Enterovirus 68 among children with severe acute respiratory infection, the Philippines. Emerg Infect Dis. 2011 Aug;17(8):1430-6.
13. Renois F, Bouin A, Andreoletti L. Enterovirus 68 in pediatric patients hospitalized for acute airway diseases. Journal of Clinical Microbiology. 2013 Feb;51(2):640-3.
14. Piralla A, Baldanti F, Gerna G. Phylogenetic patterns of human respiratory picornavirus species, including the newly identified group C rhinoviruses, during a 1-year surveillance of a hospitalized patient population in Italy. Journal of Clinical Microbiology. 2011 Jan;49(1):373-6.
15. Rahamat-Langendoen J, Riezebos-Brilman A, Borger R, van der Heide R, Brandenburg A, Scholvinck E, et al. Upsurge of human enterovirus 68 infections in patients with severe respiratory tract infections. Journal of Clinical Virology: the official publication of the Pan American Society for Clinical Virology. 2011 Oct;52(2):103-6.
16. Linsuwanon P, Puenpa J, Suwannakarn K, Auksornkitti V, Vichiwattana P, Korkong S, et al. Molecular epidemiology and evolution of human enterovirus serotype 68 in Thailand, 2006-2011. PloS one. 2012;7(5):e35190.
17. Jaramillo-Gutierrez G, Benschop KS, Claas EC, de Jong AS, van Loon AM, Pas SD, et al. September through October 2010 multi-centre study in the Netherlands examining laboratory ability to detect enterovirus 68, an emerging respiratory pathogen. Journal of Virological Methods. 2013 Jun;190(1-2):53-62.
18. World Health Organization. Regional Office for Europe. Report of the 27th Meeting of the European Regional Certification Commission for Poliomyelitis Eradication. Copenhagen: WHO; 2013. Available at: http://www.euro.who.int/en/health-topics/communicable-diseases/poliomyelitis/publications/2013/report-of-the-27th-meeting-of-the-european-regional-certification-commission-for-poliomyelitis-eradication.