



RAPID RISK ASSESSMENT

Enterovirus 68 detected in the USA, Canada and Europe

Second update, 25 November 2014

Main conclusions

- In November, France and the United Kingdom both reported sporadic cases of neurological disease involving enterovirus 68 (EV-D68) detection. As a result, ECDC has updated its rapid risk assessment on EV-D68, first triggered by reports from North America. To date, European acute flaccid paralysis (AFP)/enhanced enterovirus surveillance has not detected unusual clusters or unexpected trends. In 2014, EV-D68 has been detected in at least fifteen EU/EEA countries but no epidemic clusters of severe disease have been reported.
- Since mid-August 2014 and as of 20 November 2014, local health authorities in 47 States and the District of Columbia in the US have notified the US Centers for Disease Control and Prevention (CDC) of 1 121 laboratory-confirmed EV-D68 infections. Some regions in Canada have also been detecting respiratory illness associated with EV-D68 infection since September 2014 and, as of 4 November 2014, 214 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 AFP cases, 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 EV-D68 and the neurological illness clusters reported in several States across the US, but the virus has been circulating independently at several locations.
- To date, EU/EEA countries have not reported any unusual increase in numbers of undiagnosed acute respiratory infections, clusters of neurological disease or an increase in hospital admissions.
- The likelihood of cases of disease due to EV-D68 being laboratory-confirmed in EU/EEA countries is low because most countries do not routinely screen for enteroviruses and/or EV-D68, and the disease is not notifiable since most of the infections are caused by respiratory viruses.
- In cases of severe respiratory disease, if tests for all other respiratory pathogens are negative, or if rhino-/enterovirus is detected initially, EV-D68 should be considered as a potential cause of the disease. More systematic testing of both severe respiratory illness cases and surveys of respiratory illness in primary care/community settings for EV-D68 could be considered in EU/EEA countries to better document the incidence of disease associated with respiratory viruses in general and with EV-D68 at present.
- EU/EEA countries need to remain vigilant and consider strengthening respiratory sample screening for enteroviruses and enterovirus typing.
- EU/EEA countries should include testing for polio and other enteroviruses as part of the investigation of AFP cases, and consider strengthening AFP surveillance and/or enhanced enterovirus meningitis/neurological surveillance in order to both enhance polio surveillance and detect unusual clusters of neurological disease or trends among non-polio AFP cases. AFP cases should include the collection of cerebrospinal fluid (CSF), respiratory and faecal specimens that are tested for polio and other enteroviruses.
- Hospitals should be alert to the possibility of nosocomial infections of EV-D68, especially in immunocompromised patients.
- Based on information currently available to ECDC, the risk of increased severe cases of EV-D68 in EU/EEA countries is assessed as moderate, in light of recent reports of such cases and because the circulation of this strain in the population seems to be geographically widespread in the EU.

Source and date of request

European Commission, SANCO C3, request dated 19 November 2014.

Public health issue

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

- Has the assessment of risk to EU citizens of exposure to enterovirus 68 (EV-D68) changed since the rapid risk assessment of 15 October 2014, considering the updated epidemiological information?
- What is the risk to the EU population associated with the detection of non-polio AFP cases in the UK and France?
- 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] and updated this risk assessment on 15 October 2014 [2].

Consulted experts

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Event background information

Current epidemiological situation in the USA

From mid-August to 20 November 2014, 1 121 people from 47 States and the District of Columbia were diagnosed with respiratory illness caused by EV-D68. This is an increase of 430 cases and one additional State since the last update on 15 October 2014. 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 compared 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 [3].

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 these children had asthma or a history of wheezing. Twelve deaths have been associated with EV-D68 infection. 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. Information on prevalence in the adult population is unknown.

[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 [4,5]:

- 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 with anterior myelitis of unknown etiology, were detected by active surveillance in California. Samples from two of these cases were positive for EV-D68.

As of 20 November 2014 CDC has verified reports from 32 States of 88 recent cases involving unexplained neurological illnesses and acute onset of focal limb weakness in children and young adults ≤ 21 years of age. Based on [the case definition](#), all cases have shown a spinal cord lesion largely restricted to grey matter in a magnetic resonance image (MRI). It is not yet clear whether EV-D68 is associated with paralysis in these cases.

Current epidemiological situation in Canada

As of 4 November 2014, 214 specimens have tested positive for EV-D68. This is an increase of 139 specimens since 15 October 2014. One fatality in a young man with severe asthma has been linked to EV-D68. Health authorities in Canada are also investigating possible links to EV-D68 in cases of paralysis among children.

Epidemiological background – EV-D68 infections

Since the first isolation of EV-D68 in four children with respiratory illness in California in 1962 [6], EV-D68 infection, which is not a notifiable disease, has rarely been reported. However, similar symptoms to EV-D68 were reported during 2006–2011 from Asia, Europe and the United States [7], which also contained reports of deaths associated with EV-D68 [8]. Table 1 provides an overview of publications on EV-D68 epidemiology relating to reports of acute respiratory illness associated with EV-D68 worldwide from 1994 through 2014.

In Europe, only limited 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 [9]. There is also a report of 24 patients admitted to a university hospital, some of which needed ICU treatment [10]. All of them had mild to severe respiratory illness, some infections were nosocomial. Following the 2010 outbreak of EV-D68 in the Netherlands, through the national surveillance of ILI/ARI and national enterovirus surveillance for the period of week 1/2011 through week 40/2014, 36 EV-D68 cases were identified in a seasonal pattern; one in autumn 2011, 10 in the autumn-winter period 2011/12, five in the autumn-winter period 2012/13, and 21 since summer 2014 [11] (update for 2014 through personal communication). Furthermore, 16 patients were reported as being admitted to a university hospital in 2014, 11 children under age 18, five of which needed intensive care treatment. Three children had no underlying medical condition. Five were adults – three transplant patients and two patients with underlying lung disease [12]. Phylogenetic analysis showed identical strains to those appearing in the USA. Nosocomial infections were also reported to have occurred [12].

In France, 60 EV-D68 cases have been reported through the National Enterovirus Network (personal communication) since 2008, 63% of which had respiratory symptoms. In 2014, several respiratory cases have been notified in addition to the neurological case mentioned above [13] (and personal communication).

In the United Kingdom, 13 cases of laboratory-confirmed EV-D68 infection have been reported since 2012, mainly in young children: seven cases were reported during 2012, three in 2013, and three in 2014. Ten of the thirteen cases were diagnosed from respiratory samples, the remainder from faecal specimens [14] (and personal communication).

In Finland, several different enteroviruses have been circulating in 2014, and more than ten EV-D68 detections have been confirmed since August 2014 in the diagnostic and public health laboratories (personal communication).

The European Society of Clinical Virology and ECDC have set up a joint working group to analyse the current circulation of EV-D68 in Europe. The working group has coordinated a survey, based on retrospective and prospective typing of enterovirus and rhinovirus positive samples. Most of these samples are from paediatric cases (≤ 18 years of age), with a limited number from adult cases and at least 19 EU/EEA Member States participated in the survey. Preliminary analysis of results from the beginning of August until the end of November 2014 indicate that EV-D68 is circulating widely in Europe, in at least 15 Member States, and has caused some severe cases, but not on the scale seen in paediatric clinics and intensive care units in the USA. The complete results of the working group are pending.

EV-D68 cases with neurological symptoms in Europe

On 6 November 2014, French researchers reported a case of acute flaccid paralysis (AFP) following EV-D68 infection [13]. The patient was a four-year-old boy with onset of symptoms including headache and vomiting in September, which progressed to acute respiratory distress, hemodynamic failure, and flaccid paralysis of limbs. The boy had up-to-date immunisation against poliomyelitis and was previously healthy. He had no recent travel history outside of France and had had no contact with anyone arriving from North America. None of his family members presented with respiratory symptoms.

On 18 November, the United Kingdom notified ECDC through Early Warning and Response System (EWRS) about a case of neurological disease associated with EV-D68. The travel history and further clinical history of the patient are currently being investigated. All bacteriological and virological investigation showed negative results but EV-D68 was identified in an endo-tracheal tube sample. According to further investigations the sample has 98% similarity with one of the clades currently circulating the United States of America.

Table 1. Overview of studies where EV-D68 has been associated with respiratory disease, 1994–2014

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 from August 2006 through to April 2010	[15]
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	[8]
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.	[16]
Jul–Oct 2010	Japan (reports from local public health authorities)*	>120 cases	* Asthmatic bronchitis, pneumonia, febrile convulsions (1 case)	* 10 out of 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)	[7]
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.	[7]
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	[7]
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 ILI/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.	[9]
Oct 2008–Oct 2009	Italy (Pavia)	12 out of 1 500 samples collected	Adult and paediatric patients admitted with acute respiratory illness.	-	-	-	[17]
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.	[10]
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	[18]
2009–2012	China	7 of 1 565 samples from children (one month–14 years) positive for EV-D68. Two of 585 positive for EV-D68 in adults 17–96 years also sampled.	Wide spectrum of disease from asymptomatic to severe respiratory and even death. In children, severe pneumonia (3) and severe asthma attack (1) cases.				[19]
2011–2014	The Netherlands (nationwide)	27 EV-D68 cases in respiratory specimens in the Netherlands in week 1/2011–week 40/2014 (4579 respiratory specimens from ILI/ARI surveillance; unknown number of respiratory specimens from enterovirus surveillance)	Fever, cough,	Majority of cases in children under 20 years and adults 50–59 years of age.	Five cases had underlying disease	Samples collected as part of the national ILI/ARI and enterovirus surveillance schemes.	[11]
2014	The Netherlands (Groningen)	16 patients with EV-D68 in respiratory samples. 1896 samples tested, 39 positive for enterovirus, and 18 for EV-D68.	Children with underlying medical condition, from mild cold to severe respiratory illness. All adults with underlying medical condition.	11 children (range one month to 14 years) five adults (range 22–65 year)	Five adults (heart, lung, kidney transplant), two with lung condition. Three children with no medical condition, eight with several underlying conditions.	Routine screening for respiratory infections in tertiary university medical centre.	[12]

ECDC threat assessment for the EU

Is the increased number of cases of EV-D68 reported 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 [7]. 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 with previous years, at least in some regions. EV-D68 is not nationally notifiable in the USA and Canada. As such, it cannot be determined at this time whether the increase in the number of EV-D68 cases identified since September is unexpected, since surveillance data from previous years are not available for comparison.

A 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 [20], would suggest a greater adaptation for human infection and transmission between humans. However, sialic acid might not be the sole receptor for EV-D68 as strains from different phylogenetic clades do not haemagglutinate red blood cells carrying both alpha 2,3 and alpha 2,6 linked sialic acids (unpublished data from the Netherlands). Nevertheless, it would not explain the more severe outcomes of the EV-D68 infection. The increased number of confirmed cases in 2014 in the USA and Canada are partly due to enhanced surveillance related to the EV-D68 with improved laboratory assays.

In temperate countries, enteroviruses typically circulate with summer–autumn seasonality. EV-D68 is likely to cause a wide variety of clinical symptoms ranging from subclinical presentation to respiratory symptoms, meningitis and AFP, possibly even resulting in death. The increased detection of severe EV-D68 cases may relate to the fact that the severe cases are more likely to be investigated. There have been only a few community-based studies assessing the incidence of EV-D68 infection in the general population in persons with acute respiratory symptoms (Table 1).

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 at least in fifteen EU/EEA Member States (ESCV-ECDC working group preliminary results and [11] [13] [12]). Not all characteristics of the viruses are known, but the viruses circulating in the Netherlands belong to the same three sublineages as the viruses currently circulating in the US [11] [12]. There are ongoing studies to further characterise the circulating EV-D68 viruses, both in North America and in Europe. No EV-D68 detections have been reported from the WHO European Region through the polio laboratory network (personal communication). The severity of the current strain remains unknown. Surveillance and surveys need to be undertaken to determine the prevalence of EV-D68 resulting in disease within the community (primary and secondary care).

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

Several European countries have been reporting 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 all EU/EEA countries, but has not been detected/reported due to current diagnostics and reporting requirements. The diagnostic tests for respiratory viruses mostly focus on a limited number of viral targets, including influenza virus and RSV. Furthermore, there is often a financial constraint in performing diagnostics for a larger panel of clinically relevant viral pathogens, and the fact that enterovirus diagnostics are not included as a clinically relevant respiratory target. A number of laboratory-developed tests and commercial tests targeting respiratory viruses will not detect EV-D68 at all.

Respiratory infections of rhinoviruses or non-polio enteroviruses are not notifiable in the EU/EEA. Influenza-like illness (ILI) and/or acute respiratory infection (ARI) surveillance is in place in all EU/EEA Member States and some countries use wider respiratory virus detection panels in multiplex PCR settings to initially detect influenza virus and RSV. The same ILI/ARI surveillance can be used to also include detection of entero/rhinoviruses and the reporting of these to the national authorities. At the moment, the European Surveillance System (TESSy) can capture such detections through ILI/ARI surveillance in text format. Only Belgium, Romania and the Slovak Republic conduct syndromic surveillance of severe acute respiratory infections (SARI). Finland, France, Ireland, Spain, Sweden and the United Kingdom report laboratory-confirmed influenza infections of ICU patients to TESSy and could possibly use the same system to report other pathogens such as EV-D68.

Cerebrospinal fluid (CSF) specimens are usually tested in the diagnostic laboratories to identify any pathogen related to a severe infection with possible neurological outcomes and therefore the testing often includes testing for enteroviruses. For CSF specimens or for parallel respiratory specimens the partial enterovirus VP1 sequencing may often be performed for more than regular respiratory specimens in the clinical or diagnostic laboratory (e.g. in the AFP case in France, detection resulted from the rhinovirus PCR and VP1 sequencing from a parallel respiratory specimen, while the CSF specimens remained negative for detection of any neurotropic viruses including enteroviruses [13]).

Some EU/EEA countries conduct enhanced enterovirus surveillance [21] as part of national polio surveillance, and some countries focus on neurological presentations such as meningitis and AFP. ECDC does not yet have information on which countries have established surveillance schemes for respiratory specimens (screening for enteroviruses) or 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 and at regional level.

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?

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 the infection.

Some diagnostic laboratories based in hospitals or the community may encounter EV-D68 in clinical samples, but they would mostly detect the virus as entero- or rhinovirus positive and not attempt further characterisation. Moreover, they may not necessarily pass on their findings to the national reference centres for enteroviruses, thus reducing overall awareness of EV-D68 infections. Increasing awareness of this virus may improve referrals to reference centres.

As an interim case definition for the detection of severe paediatric cases of EV-D68 in EU/EEA countries, ECDC proposes to use:

- a paediatric (≤ 18 years) case or a case (of any age) from an immunocompromised patient or patients with an underlying lung disease with severe respiratory symptoms resulting in ICU admission;
- with human non-polio entero/rhinovirus PCR positive respiratory specimen with further specific laboratory-confirmation by sequencing for EV-D68 or a specific EV-D68 molecular assay;
- from the period 1 August 2014 onwards.

Adults may be infected as well and it is clear that EV-D68 can cause a wide range of clinical symptoms or the infection may remain asymptomatic. The case definition proposed here focuses on detection of any unusual increase in severe EV-D68 infections in children and immunocompromised persons.

For neurological patients, the [US CDC case definition and clinical management advice](#) should be used [22]. The CDC national case definition for an acute flaccid paralysis case is: acute onset of limb weakness occurring in a person ≤ 21 years of age with onset on or after 1 August, 2014, and with spinal MRI lesions largely restricted to spinal grey matter [22].

Earlier data show that some molecular detection assays for pan-enterovirus detection (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 [23]. 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 widely-used associated PCR assays would only detect EV-D68 as an enterovirus. In order to identify enterovirus 68 with absolute certainty, sequence typing is necessary, or a specific enterovirus D68 PCR should be used, neither of which are usually performed in clinical laboratories. CDC Atlanta has developed an EV-D68-specific PCR assay for simultaneous easy detection and type determination of EV-D68. Similarly, the European ESCV-ECDC working group has distributed a similar type of assay to participants in the European study. Further details for detection assays are available through the CDC as well as through the ECDC-ESCV network (for further information please contact IRV@ecdc.europa.eu).

It is likely that individual cases of EV-D68 may remain undetected in the EU/EEA because, for example, many of the entero/rhinovirus-positive clinical specimens would not be further characterised through sequencing. However, national reference laboratories that are members of the European Polio Laboratory network can offer enterovirus typing for all EU/EEA countries. Furthermore, a number of diagnostic and public health laboratories can identify, characterise and genotype a large variety of viruses including rhino- and enteroviruses.

It is important that laboratories detecting and typing EV-D68 from clinical samples publish the genomic sequences of the viruses, at least the partial (covering the BC and DE loops) or full VP1 coding portion of the genome [24], 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 [25]. 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. To supplement the AFP surveillance, some countries use enhanced enterovirus surveillance to assure that poliovirus is not circulating.

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, especially immunocompromised patients such as transplant patients and patients with an underlying lung disease [12]. It is possible that respiratory enterovirus types are more pathogenic than rhinovirus strains which could lead to more severe respiratory symptoms in acute cases [16] although rhinoviruses, especially HRV-C viruses, can also cause severe infections in small children [26] [27].

It is important that the management of underlying respiratory illnesses of children, such as asthma, is optimised according to national and European guidelines. Immunocompromised patients may be at increased risk of severe complications from EV-D68. In the USA, it has been suggested that any paediatric or adult transplant patient with respiratory symptoms should be tested for EV-D68, that lungs from donors with suspected EV-D68 should not be used, and that donation of other organs should be deferred until additional information about the incidence and duration of viraemia is known [28]. Tests should be carried out for other respiratory pathogens as well.

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. EV-D68 has been detected outside the regular autumn enterovirus season and therefore the circulation of EV-D68 may occur throughout the year [11,12].

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. In addition, nosocomial transmission has been observed within hospitals and this should be taken into account, especially with immunocompromised patients [10,12].

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 could also be occurring in the EU now or may begin 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 Regional Office for Europe from several European countries, no unusual clusters or trends were detected during August–November 2014 (personal communication). However these reports have not been received from all countries in the Region and the quality of AFP surveillance in the reporting countries is extremely variable and several countries without AFP surveillance employ enhanced enterovirus surveillance instead.

Conclusions

- In November France and the United Kingdom both reported sporadic cases of neurological disease involving enterovirus 68 (EV-D68) detection. As a result, ECDC has updated its rapid risk assessment on EV-D68, first triggered by reports from North America. To date, European acute flaccid paralysis (AFP)/enhanced enterovirus surveillance has not detected unusual clusters or unexpected trends. In 2014, EV-D68 has been detected in at least fifteen EU/EEA countries but no epidemic clusters of severe disease have been reported.
- Since mid-August 2014 and as of 20 November 2014, local health authorities in 47 States and the District of Columbia in the US have notified the US Centers for Disease Control and Prevention (CDC) of 1 121 laboratory-confirmed EV-D68 infections. Some regions in Canada have also been detecting respiratory illness associated with EV-D68 infection since September 2014 and, as of 4 November 2014, 214 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 AFP cases, 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, but the virus has been circulating independently at several locations.
- To date, EU/EEA countries have not reported any unusual increase in numbers of undiagnosed acute respiratory infections, clusters of neurological disease or an increase in hospital admissions.
- The likelihood of cases of disease due to EV-D68 being laboratory-confirmed in EU/EEA countries is low because most countries do not routinely screen for enteroviruses and/or EV-D68, and the disease is not notifiable since most of the infections are caused by respiratory viruses.
- In cases of severe respiratory disease, if tests for all other respiratory pathogens are negative, or if rhino-/enterovirus is detected initially, EV-D68 should be considered as a potential cause of the disease. More systematic testing of both severe respiratory illness cases and surveys of respiratory illness in primary care/community settings for EV-D68 could be considered in EU/EEA countries to better document the incidence of disease associated with respiratory viruses in general and with EV-D68 at present.
- EU/EEA countries need to remain vigilant and consider strengthening respiratory sample screening for enteroviruses and enterovirus typing.
- EU/EEA countries should include testing for polio and other enteroviruses as part of the investigation of AFP cases, and consider strengthening AFP surveillance and/or enhanced enterovirus meningitis/neurological surveillance in order to both enhance polio surveillance and detect unusual clusters of neurological disease or trends among non-polio AFP cases. AFP cases should include the collection of cerebrospinal fluid (CSF), respiratory and faecal specimens that are tested for polio and other enteroviruses.
- Hospitals should be alert to the possibility of nosocomial infections of EV-D68 especially in immunocompromised patients.
- Based on information currently available to ECDC, the risk of increased severe cases of EV-D68 in EU/EEA countries is assessed as moderate in the light of recent reports of such cases and because the circulation of this strain in the population seems to be geographically widespread in the EU.

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