

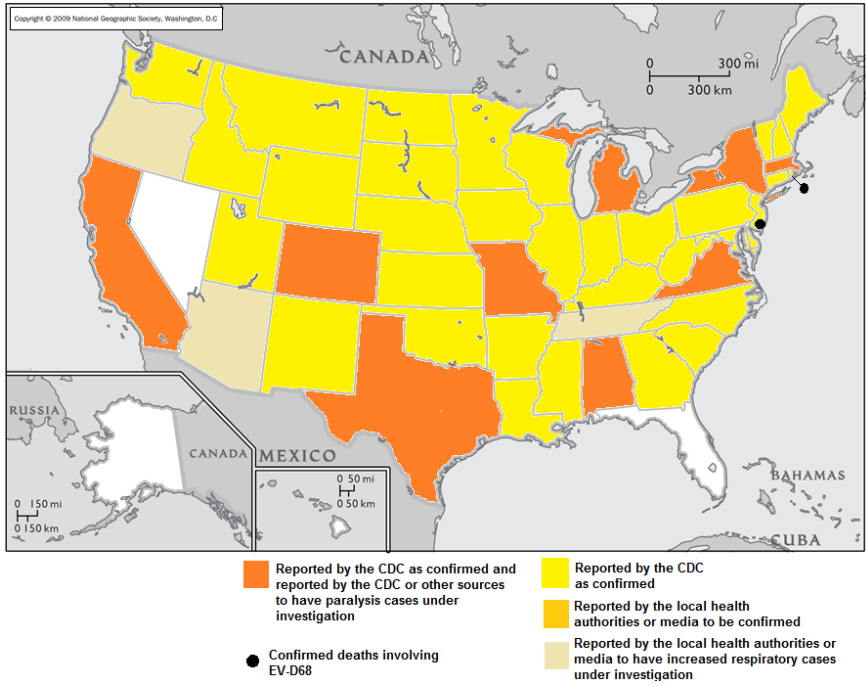


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Enterovirus EV-D68 in the United States

6 October 2014

Biosurveillance Event Report
 State, Local, Tribal, & Territorial Edition
 Public Health



States and districts reported by CDC with confirmed cases:

Alabama*	Maine	Ohio
Arkansas	Maryland	Oklahoma
California*	Massachusetts*	Pennsylvania
Colorado*	Michigan*	Rhode Island^
Connecticut	Minnesota	South Carolina
Delaware	Mississippi	South Dakota
District of Columbia	Missouri*	Texas
Georgia	Montana	Utah
Idaho	Nebraska	Vermont
Illinois	New Hampshire	Virginia*
Indiana	New Jersey^	Washington
Iowa	New Mexico	West Virginia
Kansas	New York*	Wisconsin
Kentucky	North Carolina	Wyoming
Louisiana	North Dakota	

*also reported to have paralysis cases under investigation
 ^confirmed deaths involving EV-D68

Additional states reported to be investigating respiratory clusters:

Arizona	Tennessee
Oregon	

Critical information Requirement(s):

- 1) Anomalous levels of disease
- 2) High visibility biological event

Significant Features:

Potential emerging outbreak of a rare *Enterovirus*

EXECUTIVE SUMMARY

As of 3 October 2014, 43 states and the District of Columbia have reported 538 cases (+325 since 23 September 2014) of Enterovirus D68 (EV-D68) to the U.S. Centers for Disease Control and Prevention (CDC). Most of the cases have been identified among children; however, one case was identified in an adult. This outbreak was first announced in a media conference held on 8 September 2014. In this announcement, the CDC stated that EV-D68 was detected in clusters of individuals with respiratory illness in Kansas City, Missouri and Chicago, Illinois. Many of the initial identified cases had a history of asthma or wheezing. Recent increases in cases can be attributed to awareness of this issue among health officials and the amount of time necessary for disease investigation and confirmation. Current surveillance tools for influenza-like illness may not be appropriate for the detection of EV-D68 because many of the identified cases failed to develop fever. The CDC is involved in the ongoing investigation of a possible link between EV-D68 and acute paralysis. Furthermore, the CDC has identified EV-D68 in specimens from patients who have died, but the role of EV-D68 in these deaths remains unclear. EV-D68 has rarely been reported in the U.S. since first recognized in California in 1962. Enterovirus infections are not reportable in the U.S., so the illness is likely underreported because most enterovirus infections are self-limiting and do not require medical attention. The CDC estimates that non-polio enteroviruses are very common and are responsible for 10 to 15 million U.S. infections each year.



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EVENT FEATURES

- As of 3 October 2014, the U.S. Centers for Disease Control and Prevention (CDC) had confirmed Enterovirus D68 (EV-D68) cases in 43 states and the District of Columbia affecting 538 (+325 since 23 September 2014) people. The affected regions include Alabama, Arkansas, California, Colorado, Connecticut, Delaware, District of Columbia, 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, Pennsylvania, Rhode Island, South Carolina, South Dakota, Texas, Utah, Vermont, Virginia, Washington, West Virginia, Wisconsin, and Wyoming.
- The CDC is prioritizing testing of specimens from children with severe respiratory illness; there may be more children infected with EV-D68 with milder illness that have not yet been identified.
- Similar to the initial clusters, many of the children confirmed to be infected with EV-D68 have a history of asthma or wheezing.
- Media and state public health reports have indicated that three additional states may be involved in the current EV-D68 outbreak. Increased respiratory cases under investigation are reported to be in Alabama, Tennessee, and Oregon.
- Numerous hospitals and local jurisdictions are reporting an increase in respiratory illness activity in children. Not all clusters or cases in clusters have tested positive for the presence of EV-D68. Only about half of the specimens submitted to the CDC have been positive for EV-D68; an estimated one-third of specimens have been positive for other enteroviruses/rhinoviruses.
- In a media conference held on 8 September 2014, the CDC announced the first 30 cases confirmed positive of EV-D68 in Chicago, IL and Kansas City, MO. Several more cases remain under investigation as reported by state public health departments and the media.
 - Sequencing of nasopharyngeal specimens from patients in Chicago, IL and Kansas City, MO confirmed that 30 patients, ages six months to sixteen years, from the two locations were positive for EV-D68.
 - Of those patients confirmed to be infected with EV-D68 from both locations, 21 (70%) of them are reported to have a history of asthma or wheezing and only seven (23.3%) patients are presenting with a fever. Twenty-nine of the confirmed patients have been admitted to pediatric intensive care for respiratory distress. Eight patients require artificial ventilation.
- On 29 August 2014, the Missouri Health Department issued a health alert noting an increase in respiratory illnesses in children at hospitals in Kansas City and St. Louis.
- On 23 August 2014, the University of Chicago Medicine, Comer Children's Hospital, in Chicago, IL, notified the CDC of an increased number of patients hospitalized with severe respiratory symptoms.
- On 19 August 2014, the Children's Mercy Hospital in Kansas City, MO notified the CDC of an increased number of patients hospitalized with severe respiratory symptoms. Similarly, laboratory surveillance detected an increase in nasopharyngeal specimens collected from 5-19 August 2014 testing positive for rhinovirus/enterovirus.

Possible link between EV-D68 and unexplained paralysis

- Media reports recognize cases of paralysis possibly linked to EV-D68 in an additional six states beyond those reported by the CDC. These states are Alabama, New York, Michigan, Missouri, Rhode Island, and Virginia.



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- On 12 September 2014, the Colorado Department of Public Health notified the CDC of a cluster of nine children, aged 1-18 years, with acute neurologic illness onset between 8 August and 15 September 2014. All of these children suffered fever, most with accompanying respiratory symptoms, 3-16 days prior to the onset of neurologic illness. While nasopharyngeal specimens in six of eight patients tested were positive for rhinovirus/enterovirus, no enterovirus was identified in the cerebrospinal fluid (CSF). Of those six specimens from patients positive for enterovirus, only four typed as EV-D68.
 - On 19 September 2014, the Colorado Department of Public Health released a health alert to inform clinicians of a cluster of children with acute neurologic illness and requested reports of any similar cases within the state. One additional case was reported and is under investigation.
 - On 26 September 2014, the CDC released a health advisory regarding acute neurologic illness with focal limb weakness of unknown cause in nine children in Colorado. They defined clinical criteria for cases and requested clinicians to report any patients meeting these criteria to their local and state health departments. The case definition is a patient 21 years old or younger with acute onset of focal limb weakness no earlier than 1 August 2014, and a magnetic resonance imaging (MRI) scan suggestive of spinal cord lesion primarily in the grey matter.
 - Most of the children in Colorado did show abnormalities in their spinal cord on MRI.
- In August 2012, the California Department of Public Health (CDPH) was contacted by a private local clinician requesting poliovirus testing for an unvaccinated patient with acute flaccid paralysis associated with anterior myelitis and no international travel history during the month prior to symptom onset. Two additional cases with similar symptoms of unknown etiology were reported to the CDPH within two weeks.
 - The CDPH posted official alerts for local health departments during December 2012, July 2013, and February 2014 to find additional cases of acute flaccid paralysis and uncover possible etiologies.
 - Twenty-three cases of acute flaccid paralysis with anterior myelitis of unknown etiology were identified. The CDPH Viral and Rickettsial Disease Laboratory tested nasopharyngeal swabs, rectal swabs, serum, and CSF specimens from 19 patients. No common etiology was identified among these specimens. EV-D68 was only detected in the upper respiratory tract specimens from two of these patients.

Reported deaths of patients involving EV-D68

- The CDC has identified EV-D68 in specimens from four patients who have died; the state health departments have the authority to determine when and the appropriate information to release about these patients.
 - On 3 October, the New Jersey Department of Health reported that CDC had confirmed EV-D68 in a child who had died.
 - On 1 October, Rhode Island officials reported the death of a child who died as a result of *Staphylococcus aureus* sepsis with EV-D68 co-infection.
 - It is still unclear how EV-D68 may or may not have been a contributing factor in these deaths. State and local health departments continue to investigate.

TRAVEL ALERTS



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There are no travel alerts or notices associated with this event.

CONTEXTUAL INFORMATION AND ANALYSIS

- Most of the children confirmed to be infected with EV-D68 have a history of asthma.
 - Asthma is a common respiratory complaint in children, which is often age-related and may lessen as they grow older.
 - Asthma is more prevalent in African-American children than white or Hispanic children; and higher rates of asthma seen in lower socio-economic groups.
 - The CDC reports that in 2013, an estimated 8.1% of children in the U.S. under the age of 15 were currently suffering symptoms consistent with asthma.
 - Data from 2012 indicates that in that year, children suffering asthma were most prevalent in southern states with 10.4% of children in the South currently suffering asthma and 15.4% with a history of experiencing symptoms consistent with asthma some time in their lives. Asthma symptoms were least common in the Midwest and Western states with 8.7% and 7.9% of children, respectively, suffering current asthma and 12.6% and 12.9% of children, respectively, having some history of asthma.
 - In 2012, current asthma symptoms were more common in children ages 5-11 years (11.0% within the age group). Asthma symptoms were currently exhibited in 10.5% of children ages 12-17 years and 5.4% of children ages 0-4 years. A history of asthma was more common in the older children and prevalence decreased with age.
- Increases in respiratory illnesses, especially cold and flu, are often observed in association with the time that children go back to school due to increased social contact during the school year.
 - However, an increase in respiratory illnesses was noted in the Kansas City and Chicago areas several weeks before schools resumed in many local districts.
 - Several school districts have released health advisories, guidelines, or notices in reference to EV-D68. Though, NBIC has not detected any impacts to schools or seen reports of impacts on school attendance in association with this outbreak.
- Current surveillance tools for influenza-like illness may not be appropriate for the detection of EV-D68 because many of the identified cases failed to develop fever.
- Enterovirus infections are not reportable in the U.S.; the illness is likely underreported because most enterovirus infections are self-limiting and do not require medical attention.
- Due to the awareness of this nationwide outbreak, health officials are more likely to suspect increased respiratory cases to be EV-D68 and there has been a large increase in the number of specimens tested from patients with severe respiratory illness. This increase in cases of severe respiratory illness may be caused by many different viruses that are common during this time of year, including enteroviruses.
 - It appears that EV-D68 may be the more predominant enterovirus this year. This increase in EV-D68 cases may represent an actual increase in cases or be due simply to increased attention to detection triggered by official alerts.
- Initial laboratory testing for enterovirus is a combined rhinovirus/enterovirus testing. Further sequencing is required to identify EV-D68. Most local and state public health laboratories do not have the capabilities to identify EV-D68 and the specimens must be sent to the CDC for confirmation.
- Enteroviruses are known to be one of the causes of acute neurologic disease in children. The CDC is aware of two published reports of children with neurologic illnesses confirmed as EV-D68



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infection from testing of the CSF. Enteroviruses most commonly cause aseptic meningitis, but may also cause encephalitis or, more rarely, acute myelitis and paralysis.

- Likewise, neurologic illness with muscular weakness may have a variety of noninfectious and infectious causes including Guillain-Barre syndrome, adenoviruses, West Nile virus and similar viruses, herpesviruses, and enteroviruses. Determination of the cause of neurologic illness with muscular weakness has historically been challenging, especially those due to the infectious agents.
- The CDC does note that the lack of evidence for EV-D68 detected in the CSF does not rule out that the virus did not cause damage to the spinal cord as the correct test may not have been performed or the specimen may not have been collected early enough to detect the virus.
- There are over 100 types of enteroviruses and many types have been identified routinely in patients suffering acute flaccid paralysis worldwide. However, enteroviruses are also detected routinely in children showing no signs of paralysis. Thus, paralysis due to enterovirus infection is thought to be rare; and identification of enterovirus in a patient suffering paralysis may only be an incidental finding.

U.S. GOVERNMENT RESPONSES

DHS

The National Biosurveillance Integration Center (NBIC) is monitoring the outbreak to coordinate information in response to the event. Appropriate Federal agencies are coordinating their activities and surveillance measures. The National Biosurveillance Integration System will continue to monitor the outbreak and provide situational awareness.

AFHSC

Similar to the civilian sector, the Armed Forces Health Surveillance Center (AFHSC) does not currently have any systems in place to specifically monitor for EV-D68 in military and DoD populations. However, AFHSC is providing guidance to DoD Healthcare Professionals through the ASD's office. AFHSC has detected two small outbreaks in July 2014 associated with untyped enteroviruses. No increase in activity is noted in August 2014. AFHSC does have contact with CDC in the event that further sequencing of enteroviruses is needed.

CDC

- The CDC has obtained the complete genomic sequence from seven viruses of the three strains of EV-D68 known to be circulating at this time. Comparison of the sequences of currently-circulating strains with those from previous years indicates that they are genetically-related to EV-D68 strains detected in previous years in the U.S., Europe, and Asia.
 - The CDC has submitted these sequences to GenBank so that they may be available to the scientific community for further testing and analysis.
- The CDC is actively involved in the investigation of acute flaccid paralysis possibly linked to EV-D68.
 - On 26 September 2014, the CDC released a health advisory describing acute neurologic illness in children in Colorado.
 - On 3 October 2013, the agency released MMWRs describing clusters of acute flaccid paralysis identified in Colorado and California. The agency continues to be involved in the ongoing investigation in cooperation with state public health departments.
 - The CDC has requested reporting of other similar neurologic illnesses in all states, especially cases clustered in time and place, with particular interest in characterizing the epidemiology, clinical picture and etiology of cases. The agency has received reports in



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response to this request and they are working with state and local health departments to investigate these cases.

- The CDC is working with states on the diagnosis and molecular typing for EV-D68.
 - CDC is assisting state and local health departments and clinical and state laboratories to enhance their capacity to identify and investigate these outbreaks.
 - CDC is assisting to perform diagnostic and molecular tests to improve detection of enteroviruses and enhance surveillance.
 - CDC is currently working on the development and validation of an EV-D68-specific assay for laboratory diagnosis. Once this assay is developed, they will explore options to provide test kits and protocols to state public health laboratories.
- The CDC continues to provide information to healthcare professional, policymakers, the general public, and partners in several different formats, including Morbidity and Mortality Weekly Reports (MMWRs), health alerts, websites, social media, podcasts, infographics, and presentations.
 - CDC held a media conference on 8 September 2014 to discuss and answer questions regarding recent investigations into respiratory illness clusters confirmed to be infections with EV-D68. The same day, they released a MMWR described the initial investigation in Kansas City, MO and Chicago, IL.

The CDC continues to monitor the cases of increased respiratory illness in children and [assess the situation to better understand EV-D68 and the illness caused by this virus and how widespread infections may be within states and the affected population.](#)

AGENT

Enteroviruses, of which there are over 100 types, are a genus of single-stranded RNA viruses belonging to the Picornaviridae family. This family contains Poliovirus, and non-polio enterovirus including Rhinovirus, Coxsackievirus, Echovirus, and Enterovirus. The species Enterovirus D contains five serotypes: EV-D68, EV-D70, EV-D94, EV-D11, and EV-D120. [EV-D68 has also been known as human enterovirus 68 \(HEV-68\) and human rhinovirus 87 \(HRV-87\).](#) The strains of EV-D68 that are circulating this year are not new; the CDC and state health departments have identified at least three individual strains of EV-D68 causing U.S. infections this year. The most prominent strain is related to strains detected in the U.S. in 2012 and 2013. Co-circulation of multiple strains of the same enterovirus is common.

DISEASE

Non-polio enteroviruses cause a wide range of clinical symptoms which range from mild febrile illness to [aseptic meningitis and encephalitis.](#) [Acute myelitis and paralysis are rare manifestations of enterovirus infection.](#) The average healthy adult may not get sick from most enterovirus infections or may experience mild illness, such as the common cold. Sickness is more likely in immunocompromised individuals, infants, children, or adolescents. The CDC reported that children in the first confirmed clusters of EV-D68 in Missouri and Illinois ranged in age from six weeks to 16 years with most patients having a history of asthma or wheezing. Though adults may be affected by EV-D68 and have been observed in past outbreaks, only one adult has been identified in the current identified cases. In those who develop illness, respiratory symptoms most typical with fever, runny nose, sneezing, coughing, rash, blistering around the mouth, and body aches. Less frequently, infections can cause more serious symptoms typical of viral conjunctivitis or meningitis, infections of the heart or brain, or even paralysis. The range of symptoms caused by EV-D68 is not well-characterized. However, in the patients identified in the current outbreak,



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the most prominent symptom has been difficulty breathing. Some patients have also presented with wheezing. Notably, some, but not all patients, had fever.

OCCURRENCE

Non-polio enteroviruses are very common. According to the CDC, there are between 10 and 15 million infections annually in the U.S. caused by more than 100 different Enterovirus strains. Infections are typically more common in the summer and fall months. EV-D68 is believed to be one of the less commonly-occurring enteroviruses. First recognized in California, EV-D68 has rarely been reported in the U.S. over the past 40 years. Enterovirus infections are not reportable in the U.S., so true incidence can only be estimated. The CDC does collect voluntarily-reported data in the National Enterovirus Surveillance System (NESS), which indicates 79 EV-D68 reports from 2009-2013. Because NESS is a voluntary, passive, laboratory-based system, the reports of EV-D68 are likely underestimated, though it is unknown to what extent. Furthermore, enterovirus infections can be very mild in certain individuals, making it less likely for infected people to present for testing.

SOURCE

EV-D68 is not frequently identified and the available information regarding source and transmission is limited. Humans are the only known host for these viruses.

TRANSMISSION

Non-polio enteroviruses may be transmitted through direct contact with the secretions, feces, or blister fluid from infected individuals. An infected person does not need to develop symptoms to shed the virus and be able to infect others. People can spread the infection for up to one to three weeks from their respiratory tract and several weeks in feces after they become infected.

DIAGNOSIS

Many of the symptoms caused by enteroviruses present similarly to other respiratory infections and can be easily confused or misdiagnosed. It may necessary to administer a respiratory panel to test for a range of possible respiratory infections. Standard tests used to identify respiratory diseases, such as EV-D68, identify as rhinovirus/enterovirus. Further specific testing is required to determine if the illness is EV-D68. The gold standard for this testing is genetic sequencing. Not all hospitals or local jurisdictions are capable of the level of testing required to make this determination.

Authorities are attempting to detect EV-D68 cases with ILI surveillance, though the case definition for ILI includes fever. However, the lack of fever presentation has made national surveillance of the outbreak difficult as these cases do not match the case definition for influenza-like illness and are therefore not included in that surveillance reporting.

PREVENTION, VACCINES AND TREATMENT

Because most people infected with non-polio enteroviruses never develop symptoms, it is challenging to prevent infection from spreading. Prevention strategies are the same as those recommended for most contagious diseases, which include washing your hands frequently, especially after using the bathroom or changing diapers, cleaning and disinfecting surfaces that are frequently touched, and avoiding close contact with people who are sick. This is no specific treatment for non-polio enteroviruses, rather treatment, if required, is only symptomatic. More serious, less common, non-polio enterovirus infections may require hospitalization. There are no vaccines against non-polio enteroviruses.



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