

# **Notice to Clinicians and Health Departments: Continued Vigilance Urged for Cases of Acute Flaccid Myelitis**

## **Summary**

Following the increased number of reports of acute flaccid myelitis (AFM) among children that were received by the U.S. Centers for Disease Control and Prevention (CDC) from August-October 2014, CDC has continued to receive sporadic reports of AFM. The apparent increase in AFM cases in 2014 coincided with a national outbreak of severe respiratory illness among children caused by enterovirus-D68 (EV-D68), which resulted in an increased number of children hospitalized. However, despite this close association in timing between the EV-D68 outbreak and the increase in AFM cases, an etiology for the 2014 AFM cases was not determined. As the increase in AFM cases started in August 2014, it is unclear if an increase could occur again this year, coinciding with enterovirus season. Therefore, CDC is re-emphasizing the importance of continued vigilance by clinicians for cases of AFM among all age groups, irrespective of enterovirus status. Reporting of cases will help states and CDC monitor potential increases in this illness and better understand potential causes, risk factors, and preventive measures or therapies. This notice provides the following:

- Status of the 2014 investigation;
- Information about revision to the AFM case definition;
- Recommendations for increased vigilance and reporting procedures;
- Recommendations for prompt specimen collection, and subsequent testing;
- Link to recommendations for clinical management and follow-up of patients

## **Status of the 2014 AFM Investigation**

As of July 2015, CDC has verified reports of 120 children in 34 states who developed acute flaccid myelitis that met CDC's outbreak case definition (acute limb weakness occurring in a person  $\leq$  21 years of age, with onset on or after August 1, 2014, and with spinal MRI findings largely restricted to gray matter). The median age of the children was about 7 years and almost all children were hospitalized. Most children presented with acute onset of areflexic limb weakness, usually following a respiratory or febrile illness, and about 75% of children had cerebrospinal fluid (CSF) with pleocytosis (CSF white blood cell count  $>5$  cells/mm<sup>3</sup>), often with elevated CSF protein levels. Cases were also characterized by distinctive abnormalities on spinal MRI, where pathologic changes were largely restricted to the central gray matter of the spinal cord. The findings strongly suggested an infectious (viral) process involving the spinal cord that produces a clinical illness similar to that caused by poliovirus. Many different biological specimens were collected from patients to test for various pathogens that can result in this syndrome. Although EV-D68 was the virus most commonly identified in respiratory specimens,  $<20\%$  of AFM patients had EV-D68 identified from a respiratory

specimen. Furthermore, despite extensive testing, no pathogen was consistently detected in patients' CSF. Therefore, continued vigilance and testing of specimens is needed to help to help clarify a cause and determine the frequency of AFM. A brief summary of the status of the investigation through November 13, 2014 can be found in CDC's MMWR: Acute Flaccid Myelitis Among Persons Aged  $\leq 21$  years – United States, August 1-November 13, 2014 (<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6353a3.htm>).

## Revision to AFM case definition

In June 2015, the Council of State and Territorial Epidemiologists (CSTE) adopted a standardized case definition for AFM (<http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/2015PS/2015PSFinal/15-ID-01.pdf>).

As of August 1, 2015, to be considered a case of AFM, a patient must meet the criteria below.

### **Clinical Criteria:**

An illness with onset of acute focal limb weakness and a magnetic resonance image (MRI) showing spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments, **OR** cerebrospinal fluid (CSF) with pleocytosis (white blood cell count  $>5$  cells/mm<sup>3</sup>, adjusting for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present).

#### *Case classification –*

##### **Confirmed:**

- Clinically compatible case AND
- MRI showing spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments

##### **Probable:**

- Clinically compatible case AND
- CSF showing pleocytosis (white blood cell count  $>5$  cells/mm<sup>3</sup>)

The changes in the case definition (namely, the removal of an age limit, and the addition of CSF findings to identify a “probable” case), were made for several reasons. The removal of the age limit was done to more accurately determine the overall occurrence of AFM, recognizing that certain etiologies of AFM (e.g., West Nile virus, herpesviruses) more often affect older persons than children (though children still represent the majority of AFM cases overall). The addition of CSF findings was included to add additional sensitivity to the case definition, recognizing that some patients may not undergo MRI, or MRI findings may be normal despite the presence of AFM, when the MRI is performed early in the illness.

## Recommendations for increased vigilance for cases of AFM

- CDC advises clinicians to continue reporting cases of AFM to the local and/or state health department. Patient summary forms (available at: <http://www.cdc.gov/ncird/investigation/viral/2014->

[15/health-departments.html](#)) should be completed for cases classified as confirmed or probable and submitted to CDC by email at [limbweakness@cdc.gov](mailto:limbweakness@cdc.gov) or via secure fax at 404-471-8442.

- During the 2014 investigation, the case definition focused on cases among children. The case definition has been expanded to include all ages to provide a more complete picture of the full spectrum of illness; however, the focus of increased vigilance continues to be children because AFM occurs more often in children.
- CDC also requests that cases classified as confirmed or probable be reported to state / local health departments and CDC irrespective of laboratory testing results (e.g., if a patient meets the clinical case definition for a confirmed or probable case of AFM but laboratory testing results are negative for enterovirus or any other pathogen, the case should still be reported).
- Clinicians treating patients meeting the AFM case definition should consult with their local and state health department for laboratory testing of CSF, blood, serum, respiratory, and stool specimens for enteroviruses, West Nile virus, and other known infectious etiologies.
- Health departments may contact CDC for further laboratory and epidemiologic support by phone through the CDC Emergency Operations Center (770-488-7100), or by email at [limbweakness@cdc.gov](mailto:limbweakness@cdc.gov). Confirmation of EV-D68 currently requires typing by molecular sequencing.

## **Recommendations for specimen collection and testing**

*Clinicians are advised to collect specimens from patients suspected of having AFM as early as possible in the course of illness (preferably on the day of onset of limb weakness) including CSF, whole blood, serum, stool, a nasopharyngeal aspirate, nasopharyngeal wash, or nasopharyngeal swab [with lower respiratory specimen if indicated], and an oropharyngeal swab. Early specimen collection has the best chance to yield a diagnosis. Additional instructions regarding specimen collection and shipping can be found at:*

<http://www.cdc.gov/ncird/investigation/viral/specimen-collection.html>.

- The priority of specimens for testing for AFM at CDC is: cerebrospinal fluid (CSF) >> blood (serum and whole blood) >> stool (if rule out polio testing cannot be conducted at a reference lab outside of CDC)>>nasopharyngeal aspirate, nasopharyngeal wash, nasopharyngeal swab, and oropharyngeal swab.
  - For stool specimens, CDC recommends that healthcare providers rule out poliovirus infection in cases of acute flaccid paralysis (AFP) that are clinically compatible with polio, including those with anterior myelitis. Recommendations for rule out polio testing can be found at: <http://www.cdc.gov/polio/us/hcp.html>.

## **Recommendations for clinical management and follow-up of patients**

Information to help clinicians and public health officials manage care of persons with acute flaccid myelitis that meet CDC's case definition can be found at: <http://www.cdc.gov/ncird/downloads/acute-flaccid-myelitis.pdf>.

## **For more information:**

Please visit the CDC enterovirus website (<http://www.cdc.gov/non-polio-enterovirus/>) for general information about enterovirus infections, including EV-D68, and for up-to-date guidance about infection control measures. For information about poliovirus, please visit the CDC poliovirus website (<http://www.cdc.gov/polio/us/index.html>). For information about West Nile Virus, please visit the CDC West Nile Virus website (<http://www.cdc.gov/westnile/>). State and local health departments with questions should contact the CDC Emergency Operations Center (770-488-7100).