17-ID-01

Committee: Infectious Disease

Title: Revision to the Standardized Surveillance and Case Definition for Acute Flaccid Myelitis

I. Statement of the Problem

Acute flaccid myelitis (AFM) is a syndrome characterized by rapid onset of flaccid weakness in one or more limbs and distinct abnormalities of the spinal cord gray matter on magnetic resonance imaging (MRI). Beginning in the summer and fall of 2014, an apparent increase in reports of AFM occurred in the United States, and standardized surveillance was established in 2015 to monitor this illness and attempt to estimate the baseline incidence (1). Data collected since the establishment of standardized surveillance helped with the identification of another increase in reports nationally during 2016 and has provided additional valuable information on the clinical presentation to help better characterize the clinical features, epidemiology, and short-term outcomes of cases of AFM. To facilitate interpretation of apparent increases in this syndrome, to improve the tracking of national trends, and to better define the etiologic agent(s), this position statement proposes a revision to the standardized case definition and surveillance for AFM.

II. Background and Justification

AFM is a subtype of acute flaccid paralysis (AFP). AFP is the acute onset of flaccid weakness absent features suggesting an upper motor neuron disorder. The term 'AFP' is a generalized 'umbrella' term, and includes multiple clinical entities including AFM, Guillain-Barré syndrome (GBS), acute transverse myelitis, toxic neuropathy, and muscle disorders. The annual rate of AFP among children under 15 years of age is expected to occur at approximately 1 per 100,000 children. Although AFP surveillance is commonly conducted in many countries currently still at risk for ongoing transmission of poliovirus, AFP is not a reportable condition in any U.S. state and routine surveillance and assessment for AFP is not performed. Therefore, understanding the baseline incidence and epidemiology of AFM and its public health impact in the United States is significantly limited. While AFM is most commonly attributable to poliovirus or West Nile virus and other flaviviruses, there are numerous other viruses, including non-polio enteroviruses, which may uncommonly cause AFM.

During the summer/fall of 2014, 120 confirmed cases of AFM were reported to CDC. Confirmed cases were defined as acute onset of focal limb weakness occurring on or after August 1, 2014, and an MRI showing spinal cord lesion largely restricted to gray matter, in patients ≤21 years of age. Most of the patients had distinctive abnormalities of the spinal cord gray matter on MRI and reported a respiratory or febrile illness in the days before onset of neurologic symptoms (2). Despite extensive pathogen-specific testing, no common etiology was identified. To better understand the full spectrum of AFM and determine baseline incidence, standardized surveillance for AFM was established in 2015 (1). The case definition was broadened to include patients of all ages and a probable category to capture patients demonstrating a pleocytosis (cerebrospinal fluid (CSF) white blood cells >5 mm^3) who did not have an MRI performed or had a normal MRI.

During 2015, only 21 confirmed and 3 probable cases from 17 states were reported to CDC. However, in 2016, reported cases increased to levels similar to 2014. Through December 2016, 136 confirmed and 29 probable cases have been reported from 37 states. No fatalities attributed to AFM have been reported to date.

Testing of biological specimens, including CSF, respiratory secretions, serum, and stool, continued through 2016, without identification of a common etiology (CDC, unpublished data). Thus, CDC has expanded the search for potential causes of AFM by broadening laboratory approaches that test for potential infectious and noninfectious causes, including possibly immune-mediated mechanisms.

Because polio viruses were the classic etiology of AFM in the United States prior to elimination, vaccine and travel history along with a stool test to rule out polio should always be obtained. Without a biological marker to confirm cases of AFM not associated with polio virus, classification of cases is challenging. For AFM, as with polio (3), review of case information by experts in national AFM surveillance provides consistency to classification of AFM cases.

III. Statement of the desired action(s) to be taken

1. Utilize standard sources (e.g. reporting*) for case ascertainment for acute flaccid myelitis (AFM). Surveillance for AFM should use the following recommended sources of data to the extent of coverage presented in Table III.

Table III. Recommended sources of data and extent of coverage for ascertainment of cases of Acute Flaccid Myelitis (AFM).

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	x	
Laboratory reporting	x	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)	x	
Death certificates	x	
Hospital discharge, neurology or infectious disease consult notes, MRI reports and images, or outpatient records	x	
Extracts from electronic medical records	x	
Telephone survey		
School-based survey		
Other _____		

2. Utilize standardized criteria for case identification and classification (Sections VI and VII) for acute flaccid myelitis (AFM) but do not add AFM to the *Nationally Notifiable Condition List*. If requested by CDC, jurisdictions (e.g. States and Territories) conducting surveillance according to these methods may submit case information to CDC.

Terminology:
* Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance TO local or state public health.
**Notification: process of a local or state public health authority submitting a report (case information) of a condition on the Nationally Notifiable Condition List TO CDC.

IV. Goals of Surveillance

To provide a standard case definition for states electing to perform surveillance for acute flaccid myelitis (AFM).

V. Methods for Surveillance: Surveillance for acute flaccid myelitis (AFM) should use the recommended sources of data and the extent of coverage listed in Table III.

Surveillance for acute flaccid myelitis (AFM) should use the recommended sources of data and the extent of coverage listed in Table III.

VI. Criteria for case identification

Reporting refers to the process of healthcare providers or institutions (e.g., clinicians, hospitals) submitting basic information to governmental public health agencies about cases of illness that meet certain reporting requirements or criteria. The purpose of this section is to provide those criteria to determine whether a specific illness should be reported.

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

Clinical presentation criteria:

Report any illness to public health authorities that meets all of the following criteria:

- A person with onset of acute flaccid limb weakness, AND
- A magnetic resonance image showing a spinal cord lesion largely restricted to gray matter*†, and spanning one or more vertebral segments OR
  Cerebrospinal fluid (CSF) with pleocytosis (CSF white blood cell count >5 cells/mm^3); CSF protein may or may not be elevated

  Other recommended reporting procedures
  - To provide consistency in case classification, review of case information and assignment of final case classification for all suspected AFM cases will be done by experts in national AFM surveillance. This is similar to the review required for final classification of paralytic polio cases (3).

* *Spinal cord lesions may not be present on initial MRI; a negative or normal MRI performed within the first 72 hours after onset of limb weakness does not rule out AFM. MRI studies performed 72 hours or more after onset should also be reviewed if available.*
† *Terms in the spinal cord MRI report such as "affecting mostly gray matter," "affecting the anterior horn or anterior horn cells," "affecting the central cord," "anterior myelitis," or "poliomyelitis" would all be consistent with this terminology.*

B. Table of criteria to determine whether a case should be reported to public health authorities

Table VI-B. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Reporting Disease or Condition Subtype
Clinical Evidence	
Acute onset of flaccid limb weakness	N
Magnetic resonance image (MRI) showing spinal cord lesion largely restricted to gray matter*† and spanning one or more spinal segments	O
Cerebrospinal fluid (CSF) with pleocytosis (CSF white blood cell count >5 cells/mm^3)	O

* *Spinal cord lesions may not be present on initial MRI; a negative or normal MRI performed within the first 72 hours after onset of limb weakness does not rule out AFM. MRI studies performed 72 hours or more after onset should also be reviewed if available.*
† *Terms in the spinal cord MRI report such as "affecting mostly gray matter," "affecting the anterior horn or anterior horn cells," "affecting the central cord," "anterior myelitis," or "poliomyelitis" would all be consistent with this terminology.*

Notes:
S = This criterion alone is Sufficient to report a case.
N = All "N" criteria in the same column are Necessary to report a case.
O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.
* A requisition or order for any of the "S" laboratory tests is sufficient to meet the reporting criteria.

C. Disease-specific data elements

Disease-specific data elements to be included in the initial report are listed below.

Basic demographics
Clinical information:

- Date of onset
- Limbs with acute onset of weakness
    - Description of limb weakness: limb(s) affected; weakness symmetric or asymmetric
    - Cranial nerve involvement (e.g., extraocular movement abnormalities, facial weakness)
    - Reflexes and tone (flaccid or spastic) in affected limbs
- Hospitalized (include duration)
- Date of performance of MRI (if >1 MRI performed, date of each MRI study)*
- Radiographic evidence of spinal cord lesion largely restricted to gray matter** and spanning one or more vertebral segments (if >1 MRI performed, radiographic details of each MRI)*

Laboratory data:

- Date(s) of lumbar puncture(s) (LP)
- WBC count from CSF (cells / mm^3)
- Protein level in CSF (mg/dL)

**Restricted to MRIs performed in the proximate period of the suspected AFM illness; excludes neuroimaging performed for illnesses unrelated (clinically or temporally) to AFM illness)*

***Terms in the spinal cord MRI report such as "affecting mostly gray matter," "affecting the anterior horn or anterior horn cells," "affecting the central cord," "anterior myelitis," or "poliomyelitis" would all be consistent with this terminology.*

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

Clinical Criteria
An illness with onset of acute flaccid limb weakness

Laboratory Criteria

- Confirmatory Laboratory Evidence: a magnetic resonance image (MRI) showing spinal cord lesion largely restricted to gray matter*† and spanning one or more vertebral segments
- Supportive Laboratory Evidence: cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm^3)

Case Classification

Confirmed:

- Clinically compatible case AND
- Confirmatory laboratory evidence: MRI showing spinal cord lesion largely restricted to gray matter*† and spanning one or more spinal segments

Probable:

- Clinically compatible case AND
- Supportive laboratory evidence: CSF showing pleocytosis (white blood cell count >5 cells / mm^3).

Comment

To provide consistency in case classification, review of case information and assignment of final case classification for all suspected AFM cases will be done by experts in national AFM surveillance. This is similar to the review required for final classification of paralytic polio cases (3).

***** *Spinal cord lesions may not be present on initial MRI; a negative or normal MRI performed within the first 72 hours after onset of limb weakness does not rule out AFM.*
†*Terms in the spinal cord MRI report such as "affecting mostly gray matter," "affecting the anterior horn or anterior horn cells," "affecting the central cord," "anterior myelitis," or "poliomyelitis" would all be consistent with this terminology.*

Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance
Not applicable.

B. Classification Tables

Table VII-B. Criteria for defining a case of Acute Flaccid Myelitis (AFM).

Criterion	Probable	Confirmed
Clinical Evidence		
Acute onset of flaccid limb weakness	N	N
Laboratory Evidence		
Magnetic resonance image (MRI) showing spinal cord lesion largely restricted to gray matter*† and spanning one or more spinal segments		N
Cerebrospinal fluid (CSF) with pleocytosis (CSF white blood cell count >5 cells / mm^3)	N	

***** *Spinal cord lesions may not be present on initial MRI; a negative or normal MRI performed within the first 72 hours after onset of limb weakness does not rule out AFM.*
†*Terms in the spinal cord MRI report such as "affecting mostly gray matter," "affecting the anterior horn or anterior horn cells," "affecting the central cord," "anterior myelitis," or "poliomyelitis" would all be consistent with this.*

Notes:
S = This criterion alone is Sufficient to classify a case.
N = All "N" criteria in the same column are Necessary to classify a case. A number following an "N" indicates that this criterion is only required for a specific disease/condition subtype (see below). If the absence of a criterion (i.e., criterion NOT present) is required for the case to meet the classification criteria, list the Absence of criterion as a Necessary component.
O = At least one of these "O" (One or more) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case. (These "O" criteria are alternatives, which means that a single column will have either no O criteria or multiple O criteria; no column should have only one O.) A number following an "O" indicates that this criterion is only required for a specific disease/condition subtype.

VIII. Period of Surveillance

Surveillance should be ongoing. Reporting should be provided as soon as available recommended sources of data for case ascertainment have been collected and a patient summary form has been completed.

IX. Data sharing/release and print criteria

Data may be used to measure the burden of acute flaccid myelitis (AFM).

X. Revision History

Position Statement ID	Section of Document	Revision Description
17-ID-01	Section VII. Narrative: Description of criteria to determine how a case should be classified.	CSTE National Office clarified narrative to match Table 7B by separating laboratory criteria from clinical criteria (July 2017)
15-ID-01	Table III. Recommended sources of data and extent of coverage for ascertainment of cases	ADDED additional sources of data for case ascertainment
15-ID-01	Narrative: A description of suggested criteria for case ascertainment of a specific condition.	ADDED “flaccid” to clinical presentation criteria to help with case ascertainment
15-ID-01	Narrative: A description of suggested criteria for case ascertainment of a specific condition.	DELETED text about adjusting WBC count in the presence of RBC as detail not needed for case ascertainment
15-ID-01	Narrative: A description of suggested criteria for case ascertainment of a specific condition.	ADDED text to “Other recommended reporting procedures” to explain process for classification of cases
15-ID-01	Narrative: A description of suggested criteria for case ascertainment of a specific condition.	EDITED * footnote to clarify findings on MRI
15-ID-01	Narrative: Description of criteria to determine how a case should be classified.	ADDED “flaccid” to clinical presentation criteria to help with case classification
15-ID-01	Narrative: Description of criteria to determine how a case should be classified.	DELETED text about adjusting WBC count in the presence of RBC as detail not needed for case classification
15-ID-01	Narrative: Description of criteria to determine how a case should be classified.	ADDED text to “Comment” to explain process for classification of cases
15-ID-01	Narrative: Description of criteria to determine how a case should be classified.	EDITED * footnote to clarify findings on MRI

XI. References

1. CSTE. Standardized Case Definition for Acute Flaccid Myelitis. http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/2015PS/2015PSFinal/15-ID-01.pdf.
2. Sejvar JJ, Lopez AS, Cortese MM, et al. Acute Flaccid Myelitis in the United States, August-December 2014: Results of Nationwide Surveillance. Clin Infect Dis. 2016;63:737-45.
3. CSTE. National Surveillance for Paralytic Poliomyelitis and Nonparalytic Poliovirus Infection. http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/PS/09-ID-53.pdf.

XII. Coordination

Agencies for Response

(1) Centers for Disease Control and Prevention
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Agencies for Information
N/A

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