15-ID-01

Committee: Infectious Disease

Title: Standardized Case Definition for Acute Flaccid Myelitis

I. Statement of the Problem

Acute flaccid myelitis (AFM) is a syndrome characterized by rapid onset of weakness in one or more limbs and distinct abnormalities of the spinal cord gray matter on magnetic resonance imaging (MRI). During the summer and fall of 2014, an apparent increase in reports of AFM occurring in the United States was identified. Interpreting the increase in reports of AFM in 2014 has been challenging in the absence of baseline incidence of AFM. This position statement proposes a standardized case definition for AFM.

II. Background and Justification

AFM is a subset of acute flaccid paralysis (AFP). AFP is the acute onset of weakness absent signs of spasticity or other signs indicating a central nervous system disorder, and includes AFM, Guillain-Barré syndrome (GBS), 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 is the global surveillance gold standard method of monitoring for poliomyelitis due to poliovirus, and is routinely performed in many countries, AFP is not a reportable condition in any U.S. state and routine surveillance and assessment for AFP is not performed. Therefore, understanding of the 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; other viruses, including non-polio enteroviruses, may rarely cause AFM.

In August 2014, a cluster of cases of acute limb weakness among children was identified by a group of physicians in Colorado (Pastula 2014). Most of the patients had distinctive abnormalities of the spinal cord gray matter on MRI and most had reported a respiratory or febrile illness in the days before onset of neurologic symptoms. The cluster coincided with a national outbreak of severe respiratory illness among children caused by enterovirus D68 (EV-D68) (Midgely 2014). A health advisory was issued requesting that state and local health departments report cases consistent with AFM and send specimens to CDC for testing. A standard case definition was established for reporting. A case was 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.

As of February 2015, a total of 111 cases meeting the CDC case definition have been reported from 34 states. Median age of cases is 7 years (range, 5 months to 20 years) and 60% are male. All but one case was hospitalized. At the time of this briefing, cases had been followed a median of 17 days (range, 2-101 days) after limb weakness onset and of those with information available, 62% had partially improved, 37% had not improved, and only 1% had completely recovered. However, it should be noted that it is not clear what 'partial improvement' constitutes, and many children continue to experience severe ongoing limb weakness. In addition to limb weakness, 31% of cases had cranial nerve dysfunction, 10% had altered mental status, and 4% had seizures. A total of 81% reported a preceding respiratory illness and 65% reported a febrile illness (CDC, unpublished data). No fatalities attributed to AFM have been reported.

A number of biological specimens, including cerebrospinal fluid (CSF), respiratory secretions, serum, and stool, have been received from approximately half of the cases and tested at CDC for EV-D68 and other viruses including arboviruses, adenovirus, herpesviruses, and poliovirus. One CSF specimen was positive for both EV-D68 and Epstein-Barr virus by real-time PCR, but was noted to have 1500 red blood cells, making interpretation of these results challenging. All other CSF specimens were negative. A total of 20 cases had respiratory specimens positive for enterovirus/rhinovirus, of which eight were positive for EV-

D68, 10 for a variety of rhinoviruses, and two for other enteroviruses. None of 50 stool specimens were positive for poliovirus (CDC, unpublished data).

Based on the number of cases identified during 2014 under standardized reporting, the number of cases ≤21 years of age is estimated to range from 1-10 among states (2 – 3 in the majority of states) in any given year. The number of reports is likely to double by including all ages, but this syndrome is still expected to be a rare event. By including all ages, rather than just persons ≤21 years of age, a standardized case definition will contribute to a better understanding of the etiology and epidemiology of AFM.

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

X 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		
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers)	x	
Death certificates	x	
Hospital discharge or outpatient records	x	
Extracts from electronic medical records	x	
Telephone survey		
School-based survey		
Other _____		

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X 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.

CSTE recommends that all jurisdictions (e.g. States or Territories) with legal authority to conduct public health surveillance follow the recommended methods as outline above.

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 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 focal limb weakness, AND
- A magnetic resonance image showing a spinal cord lesion largely restricted to gray matter*, and spanning one or more spinal segments OR
- Cerebrospinal fluid (CSF) with pleocytosis (CSF white blood cell count >5 cells/mm^3, may adjust for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present [fungal meningitis case definition, CDC]); CSF protein may or may not be elevated

* *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. If still unsure if this criterion is met, consider consulting the neurologist or radiologist directly.*

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

Criterion	Acute Flaccid Myelitis (AFM)
Clinical Evidence	
Acute onset of focal 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, may adjust for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present [fungal meningitis case definition, CDC])	O
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* *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. If still unsure if this criterion is met, consider consulting the neurologist or radiologist directly.*

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" (Optional) 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.

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 in affected limbs
- Hospitalized
- 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 spinal segments (if >1 MRI performed, radiographic details of each MRI)*

Laboratory data:

- Date of lumbar puncture (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. If still unsure if this criterion is met, consider consulting the neurologist or radiologist directly.*

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 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^3, may adjust for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present [fungal meningitis case definition, CDC]),

Case Classification

Confirmed:

- An illness with onset of acute focal limb weakness AND
- MRI showing spinal cord lesion largely restricted to gray matter* and spanning one or more spinal segments

Probable:

- An illness with onset of acute focal limb weakness AND
- CSF showing pleocytosis (white blood cell count >5 cells/mm^3, may adjust for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present [fungal meningitis case definition, CDC]).

***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. If still unsure if this criterion is met, consider consulting the neurologist or radiologist directly.*

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

Criterion	Probable	Confirmed
Clinical Evidence		
Acute onset of focal limb weakness	N	N
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, may adjust for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present [fungal meningitis case definition, CDC])	N	
2015 Template		

***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. If still unsure if this criterion is met, consider asking the radiologist directly.*

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).
A = This criterion must be absent (i.e., NOT present) for the case to meet the classification criteria.
O = At least one of these "O" (Optional) 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 optional criteria are alternatives, which mean 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 all necessary data have been ascertained and collected in completed form.

IX. Data sharing/release and print criteria
Data may be used to measure the burden of AFM.

X. References
1. Pastula DM, Aliabadi N, Haynes AK, et al. Acute neurologic illness of unknown etiology in children - Colorado, August-September 2014. MMWR 2014 / 10;63(40):901-2.
2. Midgley CM, Jackson MA, Selvarangan R, et al. Severe respiratory illness associated with enterovirus D68 - Missouri and Illinois, 2014. MMWR 2014 / 12;63(36):798-9.
3. Moturi EK, Porter KA, Wassilak SG, et al. Progress toward polio eradication--Worldwide, 2013-2014. MMWR 2014 / 63(21):468-72.
4. Fungal meningitis case definition, CDC: www.cdc.gov/HAI/outbreaks/clinicians/.

XI. Coordination

Agencies for Response

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