Acute Flaccid Myelitis

Surveillance and Investigation Protocol

Disease Summary
Acute Flaccid Myelitis (AFM) is a neurologic syndrome characterized by acute onset of limb weakness and distinct abnormalities of the spinal cord gray matter on magnetic resonance imaging (MRI). The diagnosis of AFM is based on a combination of clinical symptoms and specific laboratory or MRI findings.

First recognized in August 2014 after a group of children developed acute limb weakness following a respiratory or febrile illness, this illness has affected adults and other age-groups. The cause of this illness remains unknown. However, AFM cases present with illness similar to illnesses caused by viruses (enterovirus, adenovirus, West Nile Virus, herpesvirus), toxins, and genetic conditions.

Healthcare Provider Responsibilities
1. Suspect AFM when presented with a patient, particularly a child, who has sudden onset of limb weakness, loss of muscle tone and reflexes. Initiate diagnostic testing by:
   a. Obtaining MRI
   b. Testing nerve response – perform within 7-10 days after onset of weakness
   c. Collecting specimens, such as cerebrospinal fluid (CSF), blood, stool, and respiratory specimens from patients as early as possible in the course of the illness, preferably the day of onset of limb weakness. Specimens collected early in the illness have the best chance of yielding a diagnosis. For guidance on specimen collection, see Laboratory Testing.
2. Report all patients who meet the clinical case definition of AFM (see Case Classification section or visit https://www.cdc.gov/acute-flaccid-myelitis/hcp/case-definition.html), as soon as suspected regardless of laboratory results, to the state or local health department (LHD).
   b. The form should be completed by, or in conjunction with, a clinician who provided care to the patient during the neurologic illness. A form that is largely complete but has some information pending (e.g., hospital or health department laboratory results) or under investigation (e.g., polio vaccination history) should still be sent as soon as possible, and the pending results can then be provided to CDC when they become available.
   c. Send the completed form to the state or local health department as soon as possible after case identification, so cases can be evaluated in a timely manner.

Laboratory Responsibilities
1. Upon collection of appropriate specimens, prepare and store specimens as instructed on Table 1.
2. Use dry ice and recommended shipping container for shipment of specimens. The local health department or regional epidemiologist can assist in finding supplies locally.
   a. Package and ship overnight on dry ice to the CDC so that it arrives at CDC on Tuesday through Friday. Do not send specimens on Friday or over the weekend.
   b. A completed copy of the Patient Summary Form should be included with the shipment.
   c. A specimen submission form 50.34 should be completed for each specimen and included with the shipment. For Test Order Name, select “Picornavirus Special Study”. Form 50.34 can be found at https://www.cdc.gov/laboratory/specimen-submission/pdf/form-50-34.pdf.
Laboratory Testing

On December 2016, CDC 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. Despite extensive pathogen-specific testing of many specimens since 2014, CDC and others have not identified an etiology for the AFM cases. To optimize this new approach, CDC no longer performed clinical diagnostics for enteroviruses or metagenomic sequencing on specimens collected from suspect cases of AFM.

CDC has changed its collection, storage, and shipping guidance for cerebrospinal fluid, blood, and stool specimens from AFM cases. CDC is no longer requesting that respiratory specimens be collected from suspected cases of AFM. However, respiratory specimens that are positive for enteroviruses/rhinoviruses at external laboratories may be sent to CDC for typing. Stool specimens will continue to be tested to rule out the presence of poliovirus.

Because the new testing to be done at CDC uses assays that are not CLIA-approved and are not intended for clinical diagnosis, CDC will not be able to provide individual clinical reports of specific test results. Results that indicate a possible cause of AFM will be rapidly disseminated.

Table 1. Recommended Specimens and Storage Requirements for AFM

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Minimum Amount</th>
<th>Collection</th>
<th>Storage</th>
<th>Shipping</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Required</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CSF</td>
<td>1 mL</td>
<td>Spun and processed; standard cryovial tube; collect at same time or within 24 hours as whole blood</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
<td></td>
</tr>
<tr>
<td>Serum</td>
<td>0.4 mL</td>
<td>Spun and processed; Tiger/red top tube; pour serum into standard cryovial tube</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
<td></td>
</tr>
<tr>
<td>Whole Blood</td>
<td>3-5 mL</td>
<td>Unspun; lavender/green top tube (with anticoagulant); collect at same time or within 24 hours as CSF</td>
<td>Refrigerate at 4°C</td>
<td>Ship overnight on cold packs. Ship within 24-48 hours of collection*</td>
<td>Tubes should be insulated during shipping to ensure they are not in direct contact with cold pack</td>
</tr>
</tbody>
</table>
### Acute Flaccid Myelitis

**Surveillance and Investigation Protocol**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Minimum Amount</th>
<th>Collection</th>
<th>Storage</th>
<th>Shipping</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Required</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stool</td>
<td>≥1 gram whole stool</td>
<td>Collect in sterile container, no special medium required</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
<td>Two samples total, collected at least 24 hours apart, both collected as early in illness as possible and ideally within 14 days of illness onset</td>
</tr>
<tr>
<td><strong>Optional</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory – NP/OP swab</td>
<td>1 mL</td>
<td>Store in viral transport medium</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
<td>Send only if EV/RV positive for typing</td>
</tr>
</tbody>
</table>

**In the event of death, please send the following specimens, if possible**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Minimum Amount</th>
<th>Collection</th>
<th>Storage</th>
<th>Shipping</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fresh-frozen tissue</td>
<td></td>
<td>Place directly on dry ice or liquid nitrogen</td>
<td>Freeze at -70°C</td>
<td>Ship on dry ice</td>
<td>Representative sections from various organs are requested, but particularly from brain/spinal cord (including gray and white matter), heart, lung, liver, kidney, and other organs as available</td>
</tr>
<tr>
<td>Formalin-fixed or formalin-fixed, paraffin-embedded tissue</td>
<td></td>
<td>Avoid prolonged fixation – tissues should have been fixed in formalin for 3 days, then transferred to 100% ethanol</td>
<td>Room temperature</td>
<td>Ship at room temperature with paraffin blocks in carriers to prevent breakage</td>
<td>See comment above regarding frozen tissue</td>
</tr>
</tbody>
</table>

*If specimens cannot be shipped within 24-48 hours of collection, consider recollection, if feasible.*
Acute Flaccid Myelitis
Surveillance and Investigation Protocol

3. If 10 or more patient specimens are submitted, provide an electronic line listing by e-mail, using the following headers: Patient ID Number, Date of Birth, Sex, Onset Date, Fatal Y/N, Specimen ID Number, Specimen Collection Date, and Specimen Type. If culture isolate–cell line and passage number.

4. Prior to shipping, e-mail Will Weldon (ww4@cdc.gov or wweldon@cdc.gov) and limbweakness@cdc.gov regarding what is being shipped. Include the name, phone number, and e-mail address of the shipper.  

**Shipping Address:**
Dr. Will Weldon  
Centers for Disease Control and Prevention  
1600 Clifton Road, NE  
Building 17, Room 6124  
Atlanta, GA 30329  
Office: 404-639-5485

**Local Health Responsibilities**
1. Prior to the occurrence of an AFM case:
   a. Educate healthcare providers about AFM and how to detect it  
   b. Educate healthcare providers about reporting AFM, including the importance of prompt reporting.  
   c. Periodically review the laboratory supplies and materials (including shipping materials) needed for AFM testing. Make sure the healthcare providers, including the local health department have ample unexpired supplies.

2. When a suspected AFM case is reported:
   a. Request the healthcare provider to complete the Patient Summary Form. (It is best to request the healthcare provider who manages the patient’s neurologic condition.) The form can be found at [https://www.cdc.gov/acute-flaccid-myelitis/downloads/patient-summary-form.pdf](https://www.cdc.gov/acute-flaccid-myelitis/downloads/patient-summary-form.pdf)  
   b. Obtain pertinent medical records, including but not limited to history and physical, admission notes, MRI image and/or MRI reports, CSF results, and other pertinent laboratory results.  
   c. Inform DIDE about the suspected AFM case for guidance.  
   d. Collect the completed Patient Summary Form and medical records from the healthcare provider and submit to DIDE.  
      i. Pending results should not delay submission of the form. Partially completed forms are acceptable. Laboratory results can be added to the form at a later date.  
      ii. Follow up on pending results and/or partially completed forms as necessary and update DIDE as new information becomes available.

**State Public Health Responsibilities**
1. Educate LHDs about the importance of prompt detection, identification, and reporting of AFM.  
2. Coordinate education of healthcare providers with LHDs.  
3. Assist local health jurisdictions in investigating and ascertaining cases of AFM.  
4. Submit completed Patient Summary Forms to CDC by emailing limbweakness@cdc.gov (or via secure fax at 404-471-8442 or secure ftp) about each patient that meets the clinical case definition.  
5. Update AFM information sheets and protocol as new information becomes available. Develop and send out Health Alerts as necessary.  
6. Summarize surveillance data and surveillance indicators periodically and share with public health partners including CDC.
Acute Flaccid Myelitis
Surveillance and Investigation Protocol

Occupational Health
1. Assure that polio vaccination is up to date.
2. Implement measures to prevent mosquito bites. Mosquitos spread West Nile Virus, which is also a known cause of AFM.
3. Practice proper hand hygiene.

Disease Control Objectives
To reduce the occurrence of disease by investigating cases for the purpose of understanding disease epidemiology, identifying risk factors and specimen collection.

Disease Prevention Objectives
Reduce risk of disease by:
1. Practicing good personal hygiene and hand washing techniques.
2. Being up to date on all recommended vaccinations.
3. Implementing measures that control mosquito exposure and prevent mosquito bites.

Disease Surveillance Objectives
1. To identify cases promptly.
2. To determine the incidence of AFM in West Virginia.
3. To detect trends in characteristics of patients diagnosed with acute flaccid myelitis.

Public Health Significance
AFM is a very serious, yet rare illness. An increase in the number of cases in August 2014 initiated active surveillance nationwide. In 2015, there were 21 confirmed AFM cases in 16 states. In 2016, 137 confirmed cases were reported from 37 states. Numerous tests have been conducted but no specific viral or bacterial etiology has been implicated as the primary cause of AFM.

AFM primarily affects children, although it has been reported in adults. The illness typically manifests as sudden onset of asymmetrical limb weakness, loss of muscle tone and reflexes. Additional signs and symptoms vary, but the most severe symptom is respiratory failure. Recovery from AFM is slow. Currently, no deaths have been reported, although patients with serious preexisting conditions have expired following disease.

In 2016, the Centers for Disease Control (CDC) and Prevention changed the case definition of AFM (CDC removed age limit and added CSF findings to identify a “probable” case) for several reasons:

- The removal of the age limit was done to more accurately determine the overall occurrence of AFM. The case definition of AFM was 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.

- The recognition that certain etiologies of AFM (e.g., West Nile virus, herpesviruses) more often affect older people 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.

Clinical Description
Most patients will have sudden onset of limb weakness and loss of muscle tone and reflexes. Some patients, in addition to the limb weakness may experience facial drooping, facial weakness, difficulty moving their eyes, drooping eyelids or difficulty swallowing or slurred speech. Numbness or tingling is rare in patients with AFM though some patients have pain in their arms or legs. Some patients with AFM may be unable to pass urine. The most severe symptom of AFM is respiratory failure which can happen when the muscles involved with breathing become weak. This can require urgent ventilator support.

Etiologic Agent
Conditions like acute flaccid myelitis can be caused by a variety of germs including viruses such as; enteroviruses (polio and non-polio), West Nile virus, Japanese encephalitis, Saint Louis encephalitis virus, and adenoviruses. AFM is one of a number of conditions that can result in neurologic illness with limb weakness. Such illnesses can result from a variety of causes, including viral infections, environmental toxins, genetic disorders, and Guillain-Barre’ syndrome, a neurologic disorder caused by an abnormal immune response that attacks the body’s nerves.

Reservoir
The reservoir is dependent on the etiologic agent.

Mode of Transmission
Depending on the etiologic agent, the infection can be transmitted through respiratory secretions or oral and fecal route.

Adenovirus, Influenza virus, and Enterovirus-D68 (EV-D68) transmission may occur following exposure through:
- direct face-to-face contact for a period (not defined) with a case-patient who is symptomatic;
- shared confined space in close proximity for a prolonged period of time, such as ≥1 hour, with a symptomatic case-patient; or
- direct contact with respiratory secretions from a symptomatic case-patient.
Other non-polio enteroviruses can be found in the infected person’s feces, eyes, nose, and mouth secretions. Transmission may occur by:

- touching or shaking hands, with an infected person,
- touching objects or surfaces that have the virus on them, then touching your eyes, nose, or mouth before washing your hands,
- changing diapers of an infected person, then touching your eyes, nose, or mouth before washing your hands, or
- drinking water that has the virus in it.

**Incubation Period**
The incubation period is dependent on the etiologic agent.

**Period of Communicability**
The period of communicability is dependent on the etiologic agent.

**Outbreak Recognition**
West Virginia reported 2 cases of AFM in 2016. Prior to 2016, there were no reports of AFM in the state. An outbreak of AFM is suspected when there is an unusual increase in the number of cases with acute onset of focal limb weakness in one or more limbs who have distinct abnormalities of the spinal cord gray matter on magnetic resonance imaging (MRI) or who have pleocytosis in the CSF. Cases may be epidemiologically-linked by person, place, or time.

**Case Definition for Acute Flaccid Myelitis**

**Clinical Criteria:**
- An illness with onset of acute flaccid limb weakness.
- Some patients, in addition to the limb weakness may experience facial drooping, facial weakness, difficulty moving their eyes, drooping eyelids or difficulty swallowing or slurred speech.

**Epidemiologic Linkage:**
Not applicable for case definition.
Acute Flaccid Myelitis
Surveillance and Investigation Protocol

Case Classification

Probable*: To be considered a probable case, a patient must meet the following criteria:
1. Clinically compatible case, AND
2. Supportive laboratory evidence: Cerebrospinal fluid showing pleocytosis (white blood cell count >5 cells/mm³, adjusting for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present).
* Patients without an MRI performed can (at most) be classified as a probable case.

Confirmed: To be considered a confirmed case, a patient must meet the following criteria:
1. Clinically compatible case, AND
2. Confirmatory laboratory evidence; MRI showing spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments

Preventive Interventions

Currently, the etiology of AFM is uncertain, although the following interventions are good measures to prevent AFM.
1. Ensure up to date vaccinations on all recommended vaccinations, particularly the polio vaccine.
2. Minimize risk of mosquito-borne illnesses by using repellant when in high risk areas, and eliminate stagnant and standing water especially near dwellings.
3. Washing hands frequently helps stop the spread of infection. Use proper hand hygiene before touching food; after going to the bathroom, blowing your nose, changing a baby’s diaper, or touching an animal, an animal’s food, urine or feces; and before and after taking care of a sick person or a cut or wound.

There is not a specific vaccine that prevents acute flaccid myelitis but it is recommended to be up to date on your polio vaccination.

Chemoprophylaxis

There is no specific chemoprophylaxis for AFM.

Treatment

There is no specific treatment for AFM.

Neurologist may use interventions depending on case specific details. Providers can be directed to the CDC’s Acute Flaccid Myelitis: Interim Consideration for Clinical Management found at https://www.cdc.gov/acute-flaccid-myelitis/downloads/acute-flaccid-myelitis.pdf.

Surveillance Indicators

1. Report on proportion of cases with complete information.
2. Report on proportion of cases with specimens collected.
3. Report of proportion of cases with specimens tested at the West Virginia Office of Laboratory Services (OLS).
Acute Flaccid Myelitis
Surveillance and Investigation Protocol

References
1. CDC Acute Flaccid Myelitis at https://www.cdc.gov/acute-flaccid-myelitis/index.html
2. CDC Non-polio Enterovirus at https://www.cdc.gov/non-polio-enterovirus/index.html