COCA Call Information

- **For the best quality audio, we encourage you to use your computer's audio.**
- **Webinar Link:**
  https://zoom.us/j/272662215
- **If you cannot join through digital audio, you may join by phone in listen-only mode:**
  - US: +1(669)900 6833 or +1(646)876 9923
  - Webinar ID: 272 662 215
- **All questions for the Q&A portion must be submitted through the webinar system.**
- **Please select the Q&A button at the bottom of the webinar and enter questions there. Please note, your question will not be seen if submitted through the Chat button.**

Acute Flaccid Myelitis (AFM):

What Health Care Providers Need to Know

Clinician Outreach and Communication Activity (COCA)
Webinar

November 13, 2018

Continuing Education for this COCA Call

All continuing education (CME, CNE, CEU, CECH, ACPE, CPH, and AAVSB/RACE) for COCA Calls are issued online through the CDC Training & Continuing Education Online system (http://www.cdc.gov/TCEOnline/).

Those who participated in today's COCA Call and who wish to receive continuing education should complete the online evaluation by December 17, 2018 with the course code WC2922.

Those who will participate in the on demand activity and wish to receive continuing education should complete the online evaluation between December 18, 2018 and December 18, 2020 will use course code WD2922 .

Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CE's obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Continuing Education Disclaimer

- In compliance with continuing education requirements, CDC, our planners, our presenters, and their spouses/partners wish to disclose they have no financial interests or other relationships with the manufacturers of commercial products, suppliers of commercial services, or commercial supporters.
- Planners have reviewed content to ensure there is no bias. Content will not include any discussion of the unlabeled use of a product or a product under investigational use; except the following:
- Dr. Sarah Hopkins would like to disclose that she receives financial support from CDC for activities related to AFM surveillance. Dr. Hopkins would also like to disclose that she is the site principal investigator for clinical trial of SA237 in neuromyelitis optica spectrum disorder. Additionally, the unapproved use of IVIG, steroids, and plasma exchange in certain situations may be discussed during this webinar.
- CDC did not accept commercial support for this continuing education activity.

To Ask a Question

- **Using the Webinar System**
  - Click the **Q&A** button in the webinar.
  - Type your question in the **Q&A** box.
  - Submit your question.
  - Please note: your question **will not be seen** if submitted via the **chat button**.
- **For media questions, please contact CDC Media Relations at 404-639-3286 or send an email to media@cdc.gov.**
- **If you are a patient, please refer your questions to your healthcare provider.**

At the conclusion of the session, participants will be able to accomplish the following:

- Identify symptoms of AFM to look for in patients;
- Explain the process for reporting suspected AFM cases that meet the clinical criteria;
- List the types of specimens to collect from suspected cases of AFM and where to send them for testing; and
- Discuss the activities CDC is conducting as part of its investigation into AFM.

Today's First Presenter

Sarah E Hopkins, MD, MSPH
Asst. Professor of Clinical Neurology
Section Head, Multiple Sclerosis and
Neuroinflammatory Disorders
Division of Neurology
Children's Hospital of Philadelphia

Today's Second Presenter

Janell Routh, MD, MHS
Medical Officer
Acute Flaccid Myelitis Team
Centers for Disease Control and Prevention

Today's Third Presenter

Adriana Lopez, MPH
Epidemiologist
Acute Flaccid Myelitis Surveillance Team
Centers for Disease Control and Prevention

Today's Final Presenter

Manisha Patel, MD, MS
Acute Flaccid Myelitis Team Lead
Centers for Disease Control and Prevention

Acute Flaccid Myelitis

- Acute flaccid myelitis (AFM) is an illness characterized by sudden onset of flaccid weakness in one or more extremities, and is characterized by distinct grey matter lesions in the spinal cord
- CDC and external partners have been investigating AFM since 2014, when a large number of cases were noted both in the United States and globally
- AFM may be caused by different viral pathogens including: enteroviruses (including poliovirus and EV-A71), flaviviruses like West Nile virus or Japanese encephalitis virus, herpesviruses, and adenoviruses
- It is still unknown what is causing most of the AFM cases reported to CDC

AFM clinical presentation

- Over three quarters of patients describe preceding illness 1-2 weeks before weakness onset
  - Symptoms include fever, rhinorrhea, cough, vomiting or diarrhea
- Onset of weakness is rapid, within hours to a few days
- Weakness is in one or more limbs and may be accompanied by stiff neck, headache, or pain in the affected limb(s)
- Cranial nerve abnormalities may be present
  - Facial or eyelid droop
  - Difficulty swallowing or speaking
  - Hoarse or weak cry

AFM-Differential Diagnosis of limb weakness

- AFM looks like other illness, and may resemble:
  - Synovitis
  - Neuritis
  - Limb injury
  - Guillain-Barre syndrome (GBS)
  - Transverse myelitis
  - Stroke, including spinal stroke
  - Tumor
  - Acute cord compression
  - Conversion disorder
- In the late summer/early fall, with preceding viral symptoms, AFM must be high on the differential diagnosis

Initial evaluation for suspected AFM

- History-Important to collect information on any preceding illness in the past 4 weeks
  - Note respiratory and gastrointestinal symptoms, with or without fever
  - Ask about hand-foot-mouth lesions
  - Determine if there has been:
    - Decreased appetite or difficulty swallowing
    - Increased sleepiness or inactivity
    - Neck, shoulder or back pain, or headache
    - Pain in extremities
    - Bowel or bladder changes

Initial evaluation for suspected AFM

- Examination
  - Note tone and reflexes in each extremity and look for asymmetry in muscle strength and in gait
  - Conduct a thorough cranial nerve assessment looking for facial, palatal and shoulder asymmetry as well as hoarseness or hypophonia
  - Sensory exam is often normal in patients with AFM
  - Assess the ability to protect airway, and respiratory sufficiency (with negative inspiratory force, if able)

Laboratory specimen collection

- Collect specimens rapidly to increase the chance of pathogen detection
- In addition to hospital based testing, certain specimens should be routed through the state health departments to CDC for further testing and typing
- Collect for hospital based testing:
  - Nasopharyngeal and oropharyngeal swabs for respiratory multiplex testing and enterovirus (EV) PCR
  - Rectal swab for EV PCR
  - CSF: cell count with differential, protein and glucose; oligoclonal bands; PCR for EV, HZV, VZV (or a meningitis/encephalitis panel)
  - Serum: EV PCR, anti-MOG and anti-aquaporin antibodies

MR Imaging considerations for suspected AFM

- Imaging should be guided by clinical presentation and should use a 3 Tesla magnet where possible.
- Imaging within the first 72 hours of limb weakness may be normal, and should be repeated if clinically indicated
  - Axial and sagittal images are most helpful in identifying lesions
  - Because often multiple levels of the spinal cord are involved, imaging entire spinal cord is reasonable if patient is able to tolerate procedure
  - In patients with cranial nerve deficits, high cuts of brainstem should be considered or total brain MRI
  - For patients with AFM, lesions are predominantly grey matter although some cases may have white matter involvement

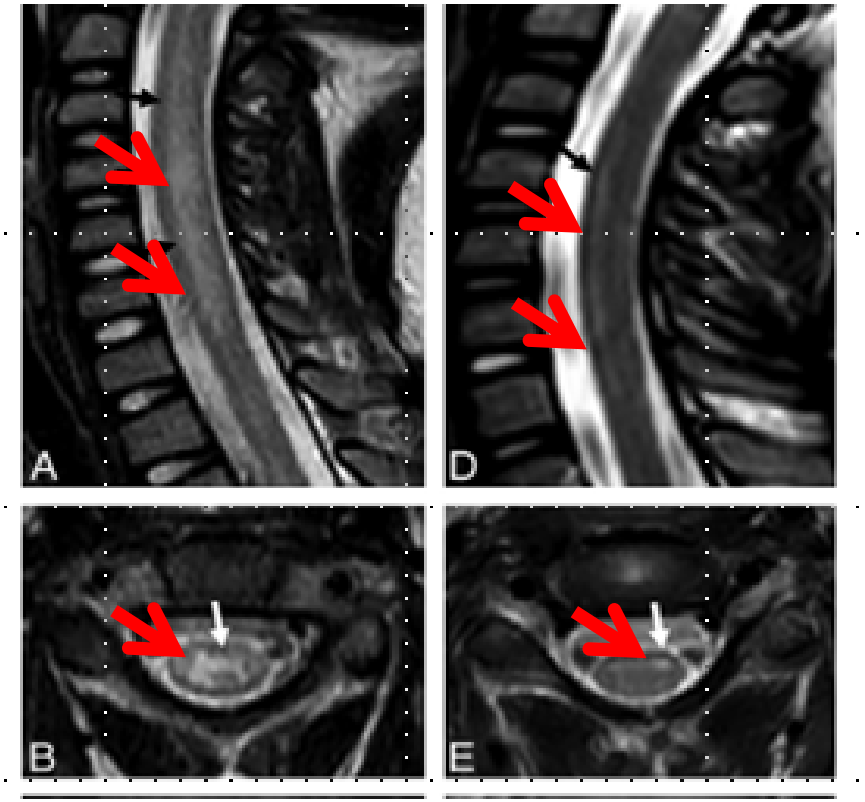
AFM MRI findings

- Grey matter lesions in > 1 spinal segment and mostly cervical
- Ventral (anterior horn) cells most commonly involved
  - Some cases have entire central grey matter involved, producing characteristic “H” pattern on axial images
  - Ventral and dorsal nerve roots may demonstrate signal abnormality
  - Conus medullaris and cauda equina involvement frequently noted
- Spinal cord lesions frequently characterized by hyperintensity on T2 and FLAIR weighted sequences and are usually non-enhancing
- Brainstem lesion involvement has been demonstrated
  - Dorsal pons and medulla mostly affected

Characteristic MRI Findings

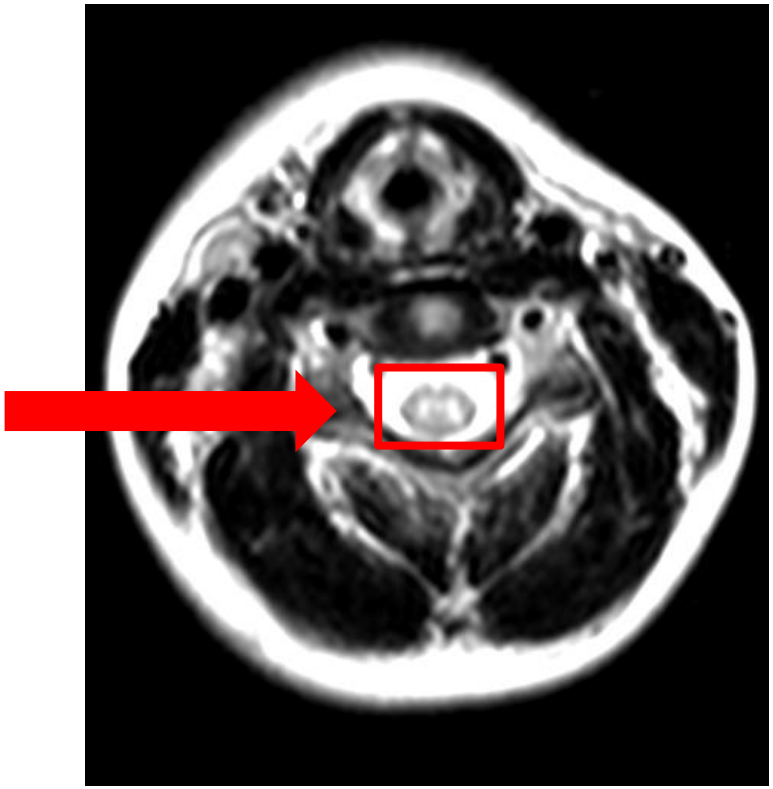
A, B. Sagittal and axial images demonstrating hyperintensity of the entire central gray matter of the thoracic spinal cord; on axial imaging, demonstrating characteristic 'H' shape pattern.

D, E. Sagittal and axial images demonstrating T2 hyperintensity confined to the left anterior horn cells (best demonstrated in E) .



*From Maloney JA et al. Am J Neuroradiol 2015;36(2):245-50

Axial Spinal Cord MR Image showing characteristic anterior horn cell lesion



When AFM is suspected, hospitalization is recommended

- Because of the potential for rapid deterioration of weakness and respiratory compromise
- To obtain early specimen collection for the possibility of pathogen detection
- For appropriate MR imaging
- For immediate consultation with neurology and infectious diseases experts to guide treatment and clinical management of this illness

TREATMENT CONSIDERATIONS FOR AFM

Treatment considerations for AFM: Challenges

- Uncertainty remains about the pathogenesis of AFM
- Diagnosis and thus treatment may be delayed
  - Mildly affected people may not seek care immediately
  - Patients may initially receive alternate diagnoses
- Systematic trials regarding many treatments have not been performed
  - Treatments usually given in combination (together or sequential) so difficult to tease apart if a single agent is effective
  - Published data limited to case reports or case-series of patients with AFM
- Consultation with experts treating AFM patients remains essential

Interim Clinical Considerations for AFM

- Created in November 2014 in response to an increase in AFM cases with input from experts in infectious diseases, neurology, critical care, virology and public health epidemiology
- In 2018, this information was formally updated using the following resources:
  - Review of the peer-reviewed published literature
  - Consultation with clinical experts in the management of AFM
- Update to the Interim Clinical Considerations is available on the CDC AFM website at: https://www.cdc.gov/acute-flaccid-myelitis/index.html

Specific treatments

- For three main treatments used for AFM, intravenous immunoglobulin (IVIG), corticosteroids, and plasmapheresis, there is not enough human evidence to indicate a preference or an avoidance for their use at this time
  - Treatment decisions should be made in conjunction with neurology and infectious diseases experts.
  - The possible benefits of using corticosteroids for spinal cord edema or white matter involvement must be balanced by the possible harm due to immunosuppression in the setting of a possible viral infection.
  - There is no indication for the use of other immunosuppressive agents in the management of AFM.

Specific treatments

- Fluoxetine is a selective serotonin reuptake inhibitor that demonstrates activity against enteroviruses
  - Both in a mouse model and retrospective case comparison of AFM patients, neither showed improvement of neurologic outcomes.
  - There is no indication that fluoxetine should be used for the treatment of AFM.
- For other anti-viral medications or interferon, there is no data to indicate their use at this time.

AFM Clinical Summary

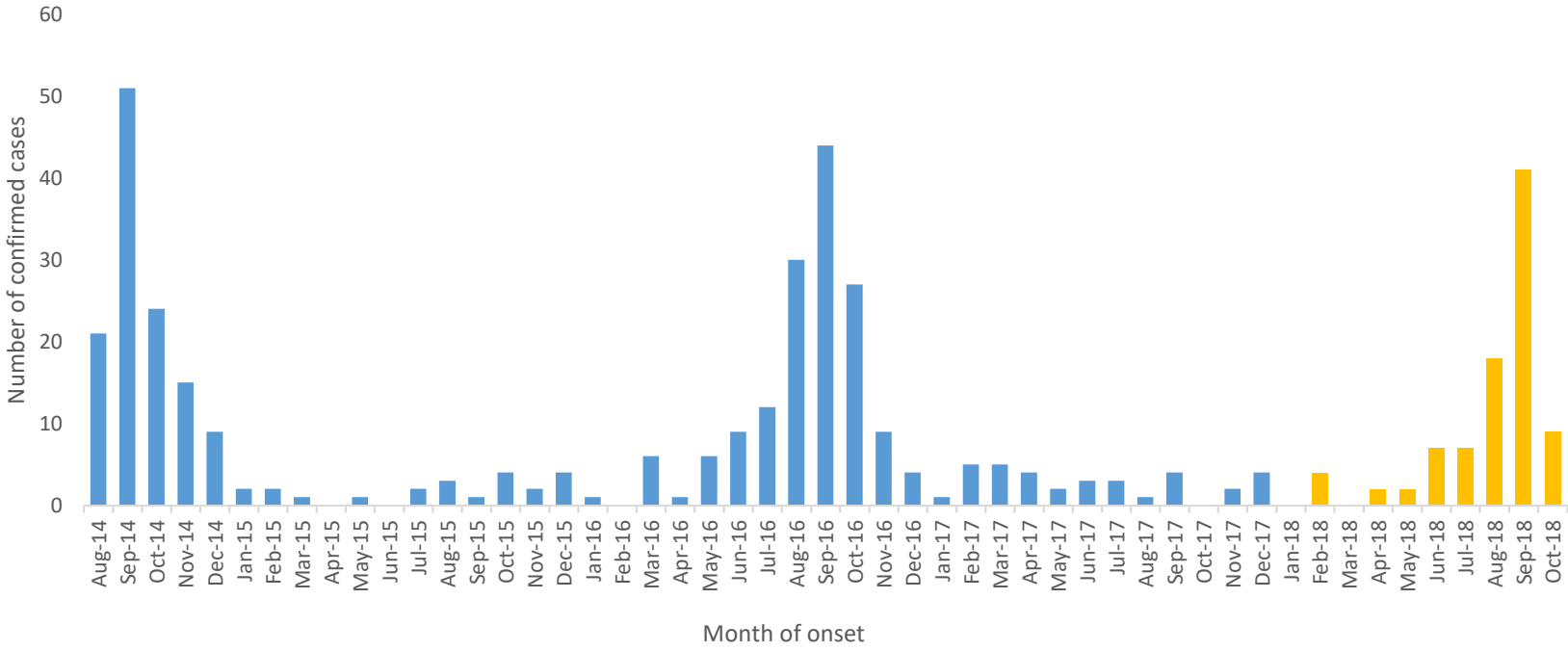
- Most patients have a preceding illness 1-2 weeks before limb weakness, and may be febrile at the time of presentation
- Clinicians should consider AFM on the differential diagnosis of patients who present with acute flaccid limb weakness, and initiate a workup including laboratory testing and MR imaging, and consultation with neurology and infectious diseases experts.
- There is currently no indication that any specific targeted therapy or intervention should be either preferred or avoided in the treatment of AFM.

CURRENT AFM EPIDEMIOLOGY AND CASE REPORTING

Surveillance for AFM

- Standardized case definition in 2015
  - **Clinical criteria: an illness with acute onset of flaccid limb weakness**
    - Confirmed case: meets clinical criteria AND MRI showing spinal cord lesion largely restricted to gray matter*† and spanning one or more spinal segments
    - Probable case: meets clinical criteria AND cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm3)
- We ask clinicians to report all patients meeting clinical criteria to their health department regardless of laboratory testing or MRI results
- Classification process is for surveillance purposes only
  - not meant to supersede the patient diagnosis or delay treatment and management decisions

Number of confirmed AFM cases reported to CDC by month of onset, August 2014-October 2018 (N = 414)



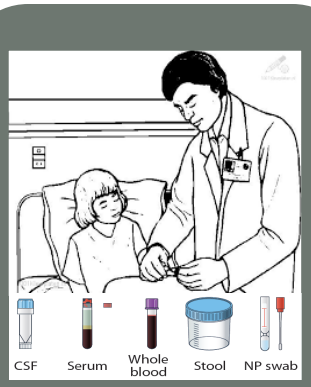
Demographic and clinical characteristics of confirmed cases

- 80 confirmed cases in 25 states
- 47/80 (59%) male
- Median age: 4 years (7 months to 32 years); 94% less than 18 years of age
- 78% with preceding respiratory illness; 98% with fever and/or respiratory illness
  - Median time between onset of preceding illness to onset of limb weakness 4.5 days (range: 0-66)
- 48% with upper limb weakness only vs 9% with lower limb weakness only
- 59% admitted to Pediatric ICUs
- CSF pleocytosis: 103 WBCs; lymphocyte predominance

CDC laboratory test results for confirmed cases of AFM (N=80)

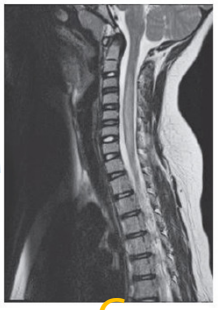
- CDC conducts enterovirus/rhinovirus (EV/RV) testing for all patients meeting the clinical criteria for AFM that are sent to CDC for testing
- From January 1-November 2, 2018, testing was performed on 125 clinical specimens from 71 patients with confirmed AFM
  - Specimens from 38 confirmed cases were positive for enteroviruses
    - CSF specimens from two patients were positive: EV-A71 (1) and EV-D68 (1)
    - Respiratory specimens from 31 patients were positive for EV-A71 (10), EV-D68 (14), and other enteroviruses (7)
- All stool specimens tested negative for poliovirus

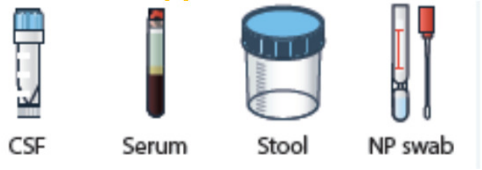
Reporting patients that meet the clinical criteria for AFM*



Clinician suspects AFM and:

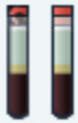
- **performs MRI**
- **obtains specimens**
- **completes case summary form**





*Clinical criteria for AFM: illness with acute onset of flaccid limb weakness

Specimens to collect from patients that meet the clinical criteria for AFM*

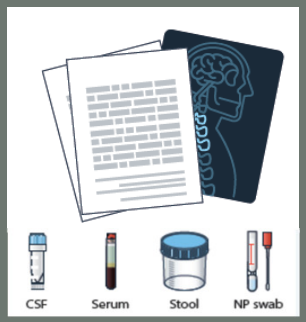
SAMPLE	AMOUNT	TUBE TYPE	PROCESSING	STORAGE	SHIPPING
CSF	1mL (collect at same time or within 24hrs of serum)	Cryovial 	Spun and CSF removed to cryovial	Freeze at -20°C	Ship on dry ice
Serum	≥0.4mL (collect at same time or within 24 hours of CSF)	Tiger/red top 	Spun and serum removed to tiger/red top.	Freeze at -20°C	Ship on dry ice
Stool	≥1 gram (2 samples collected 24hrs apart)	Sterile container 	n/a	Freeze at -20°C	Ship on dry ice. Rectal swabs should not be sent in place of stool.
Respiratory (NP)/ Oropharyngeal (OP) swab	1ml (minimum amount)	n/a 	Store in viral transport medium	Freeze at -20°C	Ship on dry ice

*Clinical criteria for AFM: illness with acute onset of flaccid limb weakness

Reporting patients that meet the clinical criteria for AFM*

Clinician suspects AFM and:
- **performs MRI**
- **obtains specimens**
- **completes case summary form**

State and Local Health Department



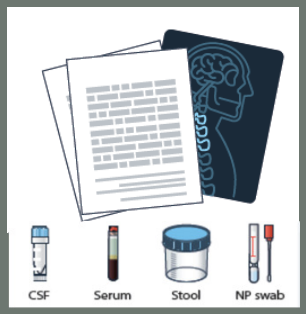
State and local health departments:
- **Reviews information from patient**
- **Collects missing data**
- **Coordinates specimen transport**

*Clinical criteria for AFM: illness with acute onset of flaccid limb weakness

Reporting patients that meet the clinical criteria for AFM*

Clinician suspects AFM and:
- **performs MRI**
- **obtains specimens**
- **completes case summary form**

State and Local Health Department



State and local health departments:
- **Reviews information from patient**
- **Collects missing data**
- **Coordinates specimen transport**

CDC

Confirmed | Probable

Case determination made by expert panel
- **Case forms**
- **MRI reports**
- **MRI images**

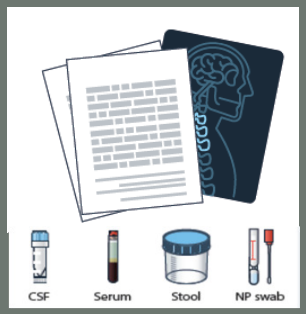
*Clinical criteria for AFM: illness with acute onset of flaccid limb weakness

Reporting patients that meet the clinical criteria for AFM*

Clinician suspects AFM and:
- **performs MRI**
- **obtains specimens**
- **completes case summary form**

State and Local Health Department

Case determination sent to clinician by State/Local Health Department



State and local health departments:
- **Reviews information from patient**
- **Collects missing data**
- **Coordinates specimen transport**

CDC

Confirmed

Probable

Case determination made by expert panel
- **Case forms**
- **MRI reports**
- **MRI images**

Laboratory Testing

Case determination sent to State/ Local Health Department by CDC

*Clinical criteria for AFM: illness with acute onset of flaccid limb weakness

CDC ACTIVITIES

What is causing AFM?

- Seasonality and presence of prodromal febrile or respiratory illness suggests infectious etiology
- AFM remains a rare event with cases scattered all over the country thus difficult to conduct evaluations
- Pathogenesis
  - Direct viral invasion of neural tissue leading to neuronal destruction
    - Limited pathology specimens to confirm this
    - No consistent pathogen isolated in specimens from confirmed cases
  - Post-infectious syndrome possible

Epidemiologic Investigations

- Data collection of clinical spectrum, exposure history, and long-term outcomes through health departments
- Retrospective MRI review to assess baseline rates of AFM
  - 5 academic medical centers; review pediatric spinal MRIs from past 10 years
  - Administrative databases to assess national baseline rates
- Syndromic Surveillance
  - Assess national trends in acute respiratory infection and AFM

Epidemiologic Studies

- Collaboration with 7 pediatric hospitals
  - Active case finding and retrospective review to establish baseline rates
  - Long-term follow-up of AFM cases
  - Year-round, prospective respiratory and gastrointestinal illness surveillance and laboratory sampling conducted at 7 pediatric tertiary care centers since 2017
- Case control studies to evaluate risk factors
  - Will require a multi-jurisdictional approach to achieve adequate sample sizes

Selected CDC Laboratory activities

- Diagnostic
  - Continuing to provide pathogen-specific testing for enteroviruses on clinical specimens including CSF, nasopharyngeal and stool samples
  - External lab results critical to inform etiology; data collection ongoing
  - Using metagenomics sequencing approaches to identified pathogens not currently considered in specifically targeted approaches
- Immunologic
  - Developing assays to look for biomarkers associated with AFM
  - Investigating post-infectious immune pathology as a mechanism for AFM

Provider Resources

- Provider Tool Kit
  - Editable Job-aid for providers where health departments can rebrand
  - Frequently asked questions document for health departments share with providers
  - Standardized slide deck currently being updated
- Updating website based on comments and questions from the general public, providers and health departments
- AFMInfo@cdc.gov
  - Inquiry and information portal

AFM Task Force

- National experts in multiple disciplines (clinical, epidemiology, immunology, pathology, infectious diseases, neurology, pediatrics, host genetics/genomics, and laboratory aspects of virology and molecular biology)
- Objectives:
  - Develop research agenda to further characterize the pathogenesis of AFM and develop hypotheses about potential etiologies
  - Review and update clinical guidance on the management of patients with AFM

Summary of CDC investigation

- Despite the increase in cases this year, AFM is still rare
  - As of November 13, 2018, CDC has confirmed 90 cases this year and 414 AFM cases since August 2014
- There has been limited detection of pathogens in the CSF of these AFM cases which would be good evidence of the cause for the patient's condition
- CDC continues to investigate all potential causes of AFM, including viral infections like enteroviruses
- CDC and partners are working to better characterize the risk factors for AFM and why some people develop this condition and others do not

Your role is important

- All clinicians involved in patient care may encounter a patient with acute flaccid limb weakness and understanding the next steps in the patient workup is critical
- Be vigilant for AFM and report patients with acute flaccid limb weakness to your local/state health department

Thank you

For additional information visit:
www.cdc.gov/acute-flaccid-myelitis

Contact CDC at: AFMinfo@cdc.gov

Today's webinar will be archived

When: A few days after the live call

What: All call recordings (audio, webinar, and transcript)

Where: On the COCA Call webpage

https://emergency.cdc.gov/coca/calls/2018/callinfo_111318.asp

To Ask a Question

- **Using the Webinar System**
  - Click the Q&A button in the webinar;
  - Type your question in the Q&A box (please do not submit questions via the "chat" button, as it will not be seen by the moderator).
  - Submit your question.
  - CDC Media: media@cdc.gov or 404-639-3286.
  - Patients, please refer your questions to your healthcare provider.

Continuing Education for this COCA Call

All continuing education (CME, CNE, CEU, CECH, ACPE, CPH, and AAVSB/RACE) for COCA Calls are issued online through the CDC Training & Continuing Education Online system (http://www.cdc.gov/TCEOnline/).

Those who participated in today's COCA Call and who wish to receive continuing education should complete the online evaluation by December 17, 2018 with the course code WC2922.

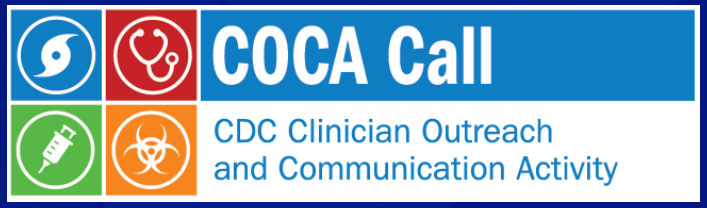
Those who will participate in the on demand activity and wish to receive continuing education should complete the online evaluation between December 18, 2018 and December 18, 2020 will use course code WD2922 .

Continuing education certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CE's obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

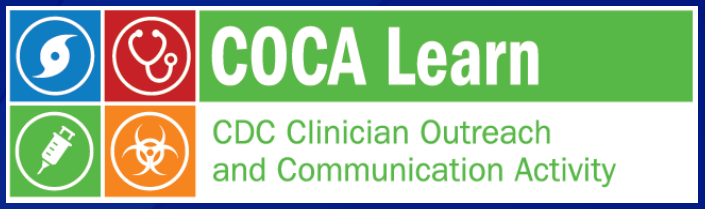
Upcoming COCA Call

Topic: Multi-State Hepatitis A Outbreak
Date: Thursday, November 29, 2018
Time: 2:00-3:00pm ET

COCA Products & Services



Promotes COCA Calls and contains all information subscribers need to participate in COCA Calls. COCA Calls are done as needed.

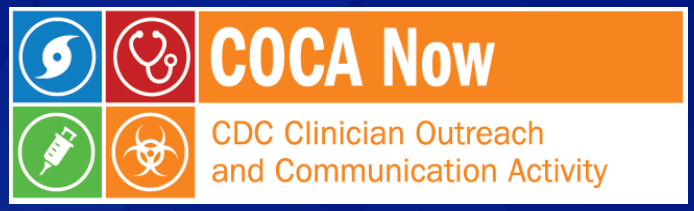


Monthly email that provides information on CDC training opportunities, conference and training resources located on the COCA website, the COCA Partner Spotlight, and the Clinician Corner.

Provides comprehensive CDC guidance so clinicians can easily follow recommendations.

COCA Products & Services

Monthly email that provides new CDC & COCA resources for clinicians from the past month and additional information important during public health emergencies and disasters.



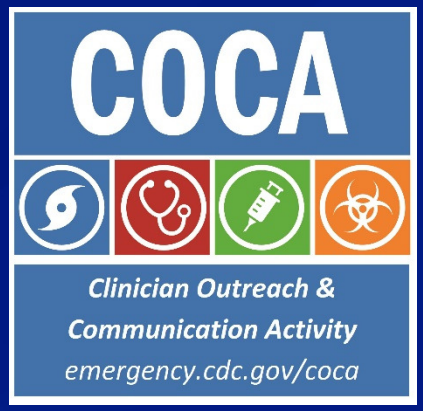
Informs clinicians of new CDC resources and guidance related to emergency preparedness and response. This email is sent as soon as possible after CDC publishes new content.

CDC's primary method of sharing cleared information about urgent public health incidents with public information officers; federal, state, territorial, and local public health practitioners; clinicians; and public health laboratories.

Join COCA's Mailing List!

Receive information about:

- **Upcoming COCA Calls**
- **Health Alert Network notices**
- **CDC public health activations**
- **Emerging health threats**
- **Emergency preparedness and response conferences and training opportunities**



http://emergency.cdc.gov/coca

Join Us on Facebook!

Thank you for joining!

Centers for Disease Control and Prevention
Atlanta, Georgia
http://emergency.cdc.gov/coca