



Acute Flaccid Myelitis: What Healthcare Providers Need to Know in 2020

Janell Routh, MD MHS

Medical Officer and Program Lead
AFM and Domestic Poliovirus Team

Sarah Kidd, MD MPH

Medical Officer
AFM and Domestic Poliovirus Team

Division of Viral Diseases

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Adriana Lopez, MPH

Epidemiologist
AFM and Domestic Poliovirus Team

Alexandra Hess, PHD

Health Communications Specialist
Northrop Grumman Corporation (Contractor)

Conflict of interest and disclaimer

Conflict of Interest

Presenters have no conflict of interest to disclose.

Disclaimer

This presentation will include the discussion of off-label treatment options not approved by the U.S. Food and Drug Administration (FDA) for use in the treatment of acute flaccid myelitis (AFM). Currently, there are no FDA-approved treatments for AFM.

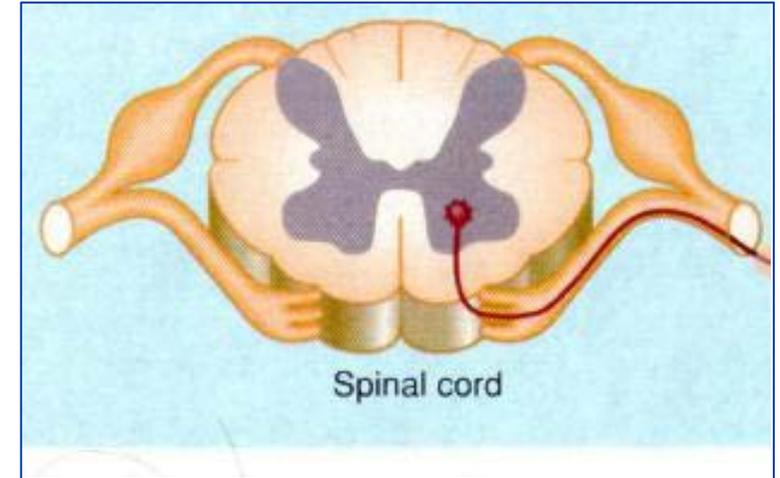
Webinar outline

- Introduction
- Clinical Overview of AFM
 - How to Recognize AFM
 - Initial Evaluation
 - Diagnostic Studies
 - Clinical Management of AFM
- Reporting of AFM
- Epidemiology
- AFM Resources for Healthcare Professionals

Introduction

Acute flaccid myelitis (AFM)

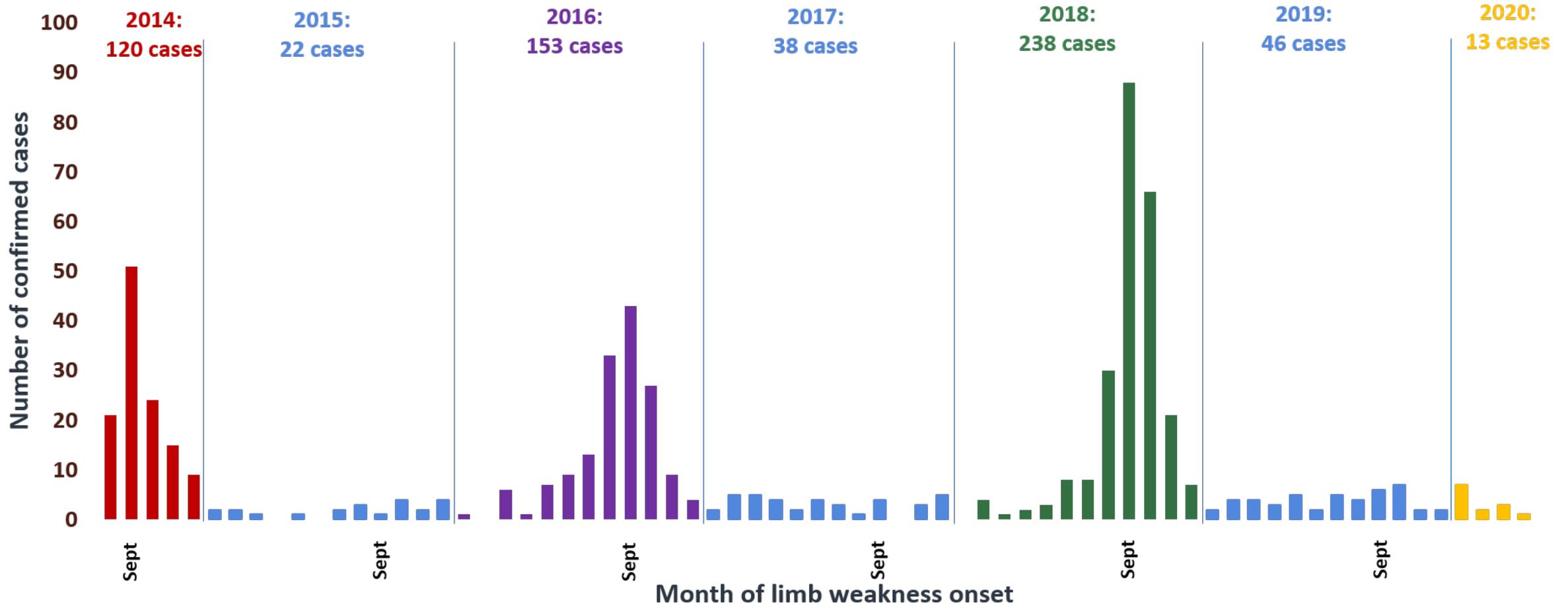
- The term was created in 2014 to describe illness in patients with sudden onset of limb weakness and lesions in the spinal cord gray matter
- Clinical presentation is similar to poliomyelitis
- Mostly children are affected
- Viral causes:
 - non-polio enteroviruses (EVD68, EVA71)
 - flaviviruses (West Nile virus, Japanese encephalitis virus)
 - herpesviruses
 - adenoviruses



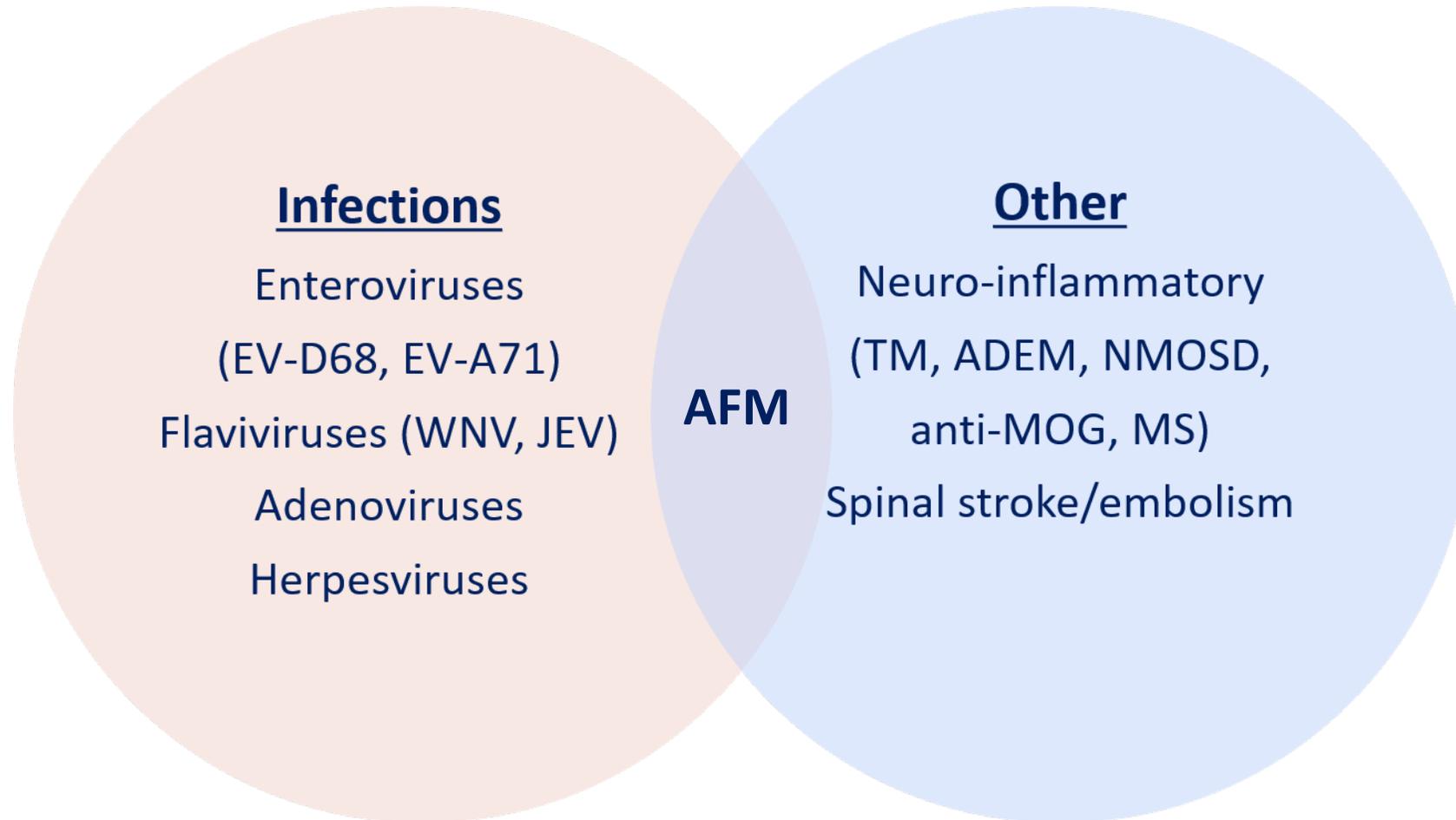
Caption: Cross-section of the spinal cord showing the gray matter and lower motor neurons affected in AFM.

National increase in AFM cases every 2 years since 2014

Number of confirmed reported AFM cases, Aug 2014 – June 2020 (n=630)

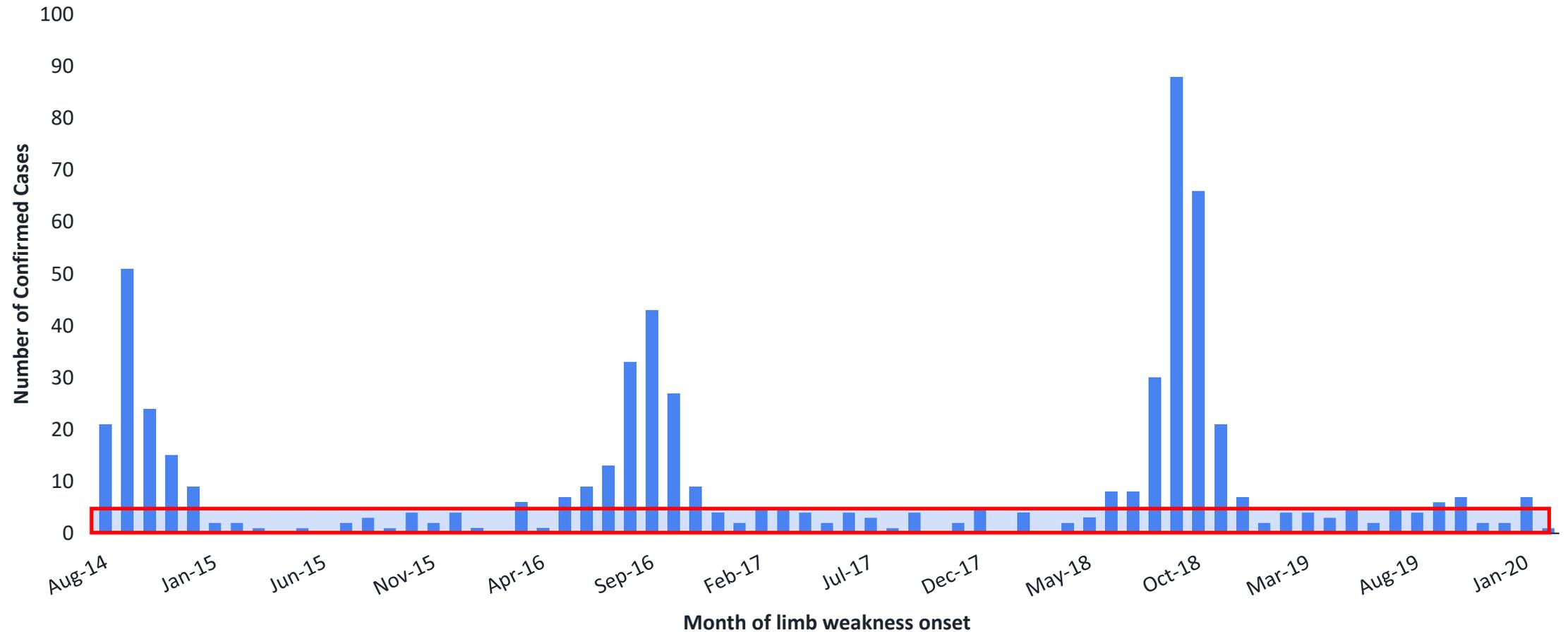


Causes of AFM



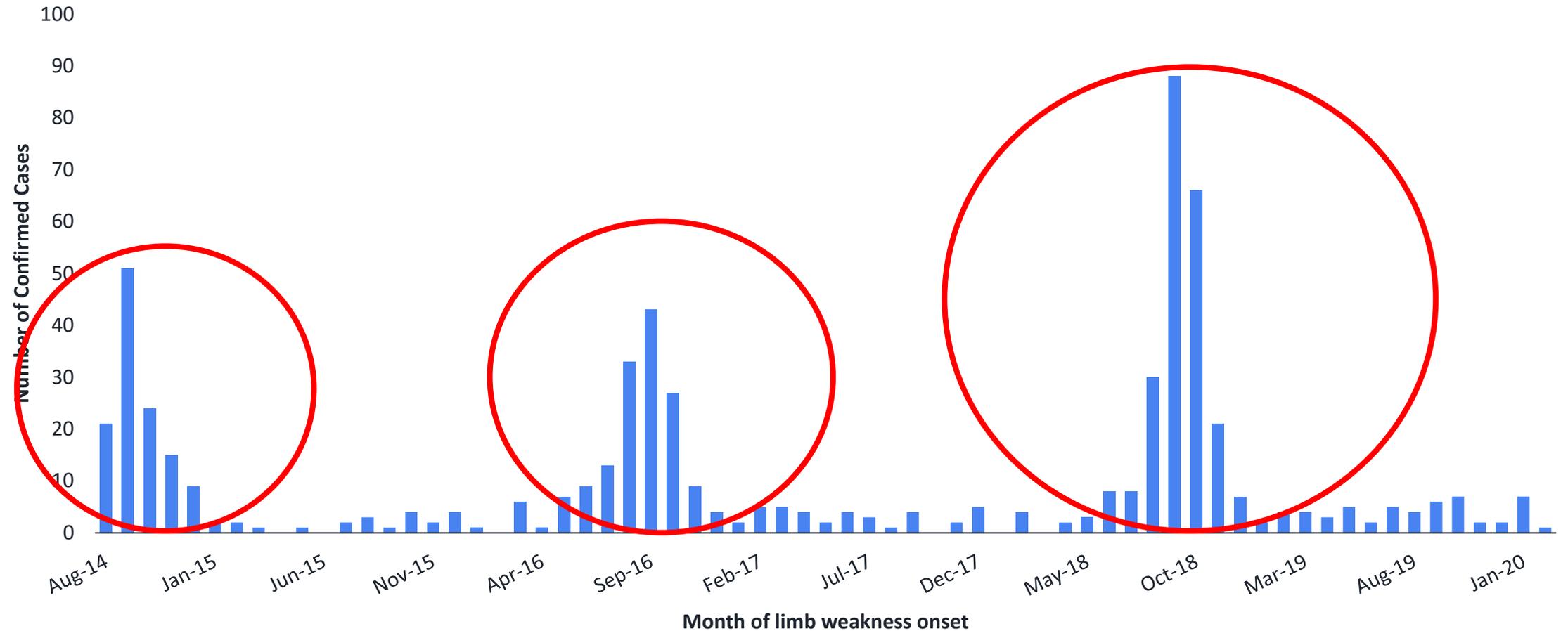
U.S. surveillance shows a consistent baseline rate of AFM

Number of confirmed reported AFM cases, Aug 2014 – May 2020 (n=625)



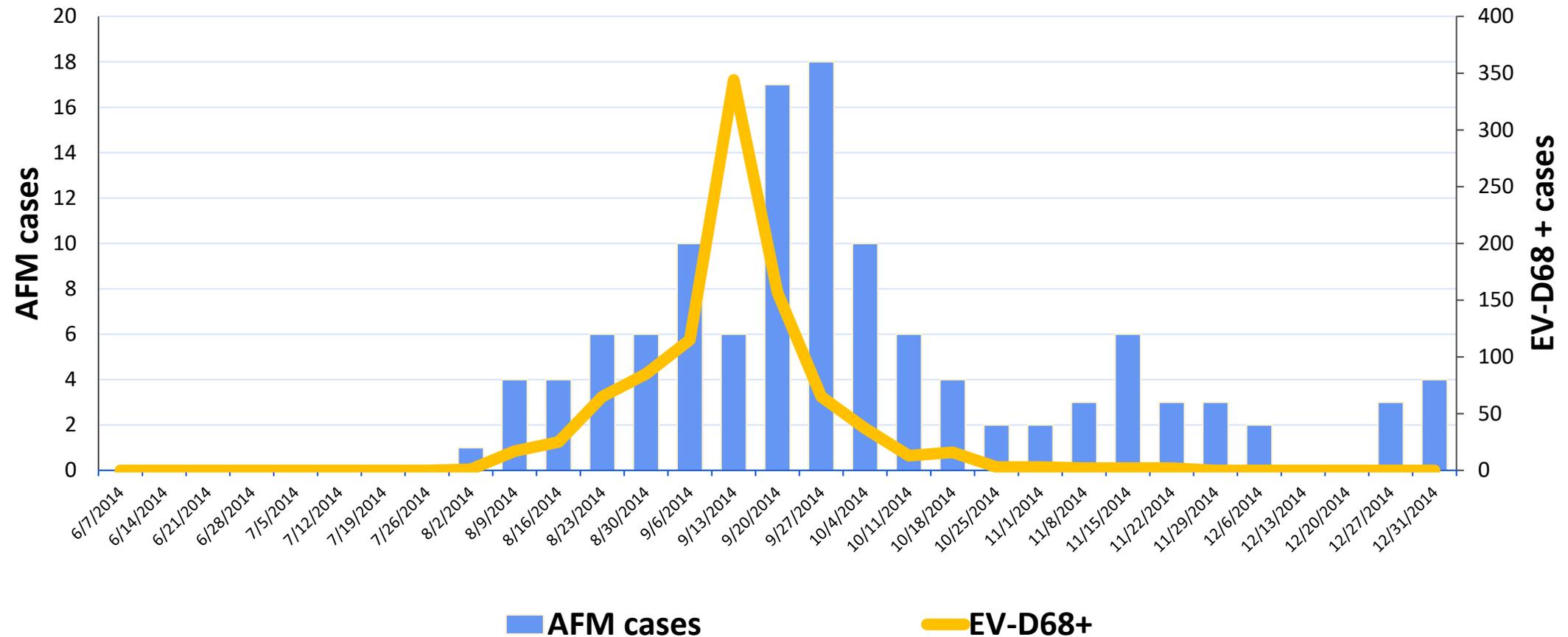
What is causing the biennial peaks in AFM?

Number of confirmed reported AFM cases, Aug 2014 – May 2020 (n=625)



Temporal association between AFM and EV-D68 in the United States, 2014

AFM and EV-D68 Respiratory Cases By MMWR Week,
01 August 2014 – 31 December 2014 (n=120)



How to Recognize AFM

What clinical characteristics would make you suspect AFM?

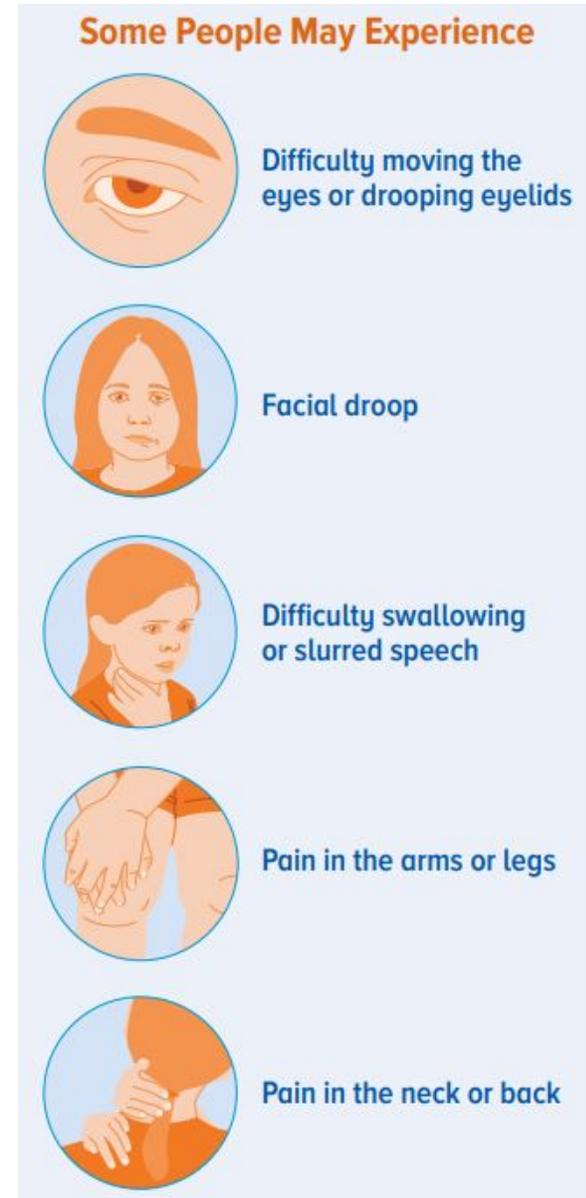
AFM clinical presentation

- Most patients had preceding febrile illness 1-2 weeks before the **sudden onset of flaccid limb weakness**
 - Frequently respiratory or gastrointestinal illness with symptoms of fever, rhinorrhea, cough, vomiting or diarrhea
- Onset of weakness is rapid
 - Within hours to a few days
- Weakness is in one or more limbs
 - More proximal than distal
- Loss of muscle tone and reflexes



AFM clinical presentation (2)

- Cranial nerve abnormalities may be present
 - Facial or eyelid droop
 - Difficulty swallowing or speaking
 - Hoarse or weak cry
- Some patients may complain about stiff neck, headache, or pain in the affected limb(s)
- Uncommonly, people may also:
 - Have numbness or tingling in the arms or legs



AFM clinical presentation (3)

- The most severe complications of AFM are:
 - **Respiratory failure**, requiring mechanical ventilation
 - **Serious neurologic manifestations** such as body temperature changes and blood pressure instability that could be life threatening



Clinicians should immediately admit patients to the hospital because AFM can progress rapidly and require urgent medical intervention, like assistance with breathing.

Differential diagnosis of flaccid limb weakness

AFM may resemble:

- Synovitis
- Neuritis
- Limb injury
- Guillain-Barre syndrome (GBS)
- Transverse myelitis
- Stroke, including spinal stroke
- Tumor
- Acute cord compression
- Conversion disorder

- AFM must be high on differential diagnosis in **late summer or early fall**, especially in patients with preceding viral symptoms.
- Careful neurological examination, laboratory testing, and MRI of the spine and brain can help guide diagnosis

Initial Evaluation

What to look for and ask about in a patient presenting with acute flaccid weakness?

Medical history

- Collect information on any illness in the past 4 weeks
- Note respiratory and GI symptoms, with or without fever
- Ask about hand-foot-mouth lesions (possible EV-A71 or similar viral infection)

Focused, age-appropriate assessment and questions to evaluate limb function impairment(s)

- Young children or their parents may not describe their limb function impairment as “weakness”

New inability or difficulty	Example questions to ask about limb function
To use arm(s)/hand(s)	<ul style="list-style-type: none">- Can they feed themselves?- Are they suddenly using one limb less or refusing to use one limb?
To raise arm(s) above the head	<ul style="list-style-type: none">- Can they put on or take off a T-shirt?- Can they throw a ball overhead?
To walk	<ul style="list-style-type: none">- Are they limping or dragging a leg?- Are they falling often while walking?
To get up unassisted from sitting or squat	<ul style="list-style-type: none">- Can they put on or take off pants?- Can they get out of bath tub unassisted?

Additional signs and symptoms

- Ask about additional signs and symptoms, including:
 - Difficulty holding their head up
 - Decreased appetite or difficulty swallowing
 - Headache or neck, shoulder, or back pain
 - Patients often complain of this prior or concurrent to weakness
 - Pain in extremities
 - Increased sleepiness or inactivity
 - Bowel or bladder changes, particularly constipation

Physical exam

Perform physical exam along with an age-appropriate neurological exam.

- Neurological examination should include documentation of:
 - Muscle tone (flaccid/loose vs spastic/tight and firm)
 - Muscle strength (full strength, move against gravity with some resistance/pressure, move against gravity but with no resistance/pressure, or little limb movement but not against gravity, no muscle movement at all)
 - Reflexes in each extremity (hypo-, hyper, or absent)
 - Any cranial nerve deficiencies such as for facial, palatal and shoulder asymmetry, hoarseness or hypophonia and dysphagia (if possible)
 - Note: Sensory exam is often normal in patients with AFM

Physical exam (cont.)

- Assess the patient's ability to protect their airway
 - Document respiratory sufficiency
 - Negative inspiratory force may be used if the child is old enough and able to cooperate
- Check for autonomic manifestations
 - Blood pressure lability
 - Body temperature instability

Knowledge Check 1

Which of the following can be symptoms of AFM?

- a) Sudden onset of arm or leg weakness
- b) Facial droop or weakness
- c) Difficulty moving eyes or drooping eyelids
- d) Difficulty with swallowing or slurred speech
- e) All of the above

- Answer: **e) All of the above**

Diagnostic Studies

What specimens and tests are needed for the initial AFM work-up?

Initial neurodiagnostic studies

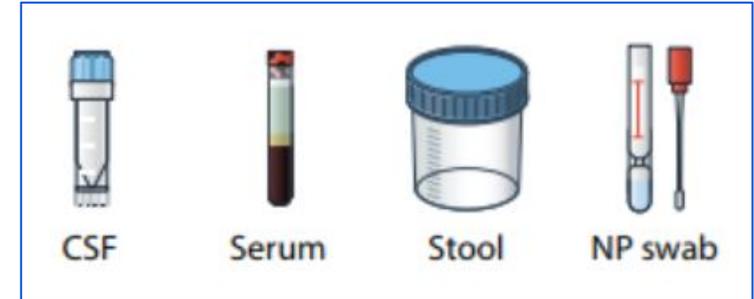
■ Laboratory Tests

- Cerebrospinal fluid (CSF)
 - cell count with differential, protein and glucose; oligoclonal bands; meningitis/encephalitis PCR panel
- Serum
 - EV PCR, anti-MOG (myelin oligodendrocyte glycoprotein) and anti-aquaporin antibodies, HSV, EBV, WNV
- Stool/Rectal swab for EV PCR
- Nasopharyngeal (NP) and/or oropharyngeal (OP) swabs
 - respiratory multiplex testing and enterovirus (EV) PCR

■ Neuroimaging

- MRI of the spine and brain

■ Consider additional pathogen-specific testing (e.g., Lyme) based on seasonality, exposures, and geography



Note: Some of these studies may require sedation, depending on child's age

- Coordinate the procedures to avoid repetitive sedation if possible
- Monitor respiratory status continuously

Laboratory specimen collection

- Rapid specimen collection increases the chance of pathogen detection
- Specific testing for AFM should be done in consultation with neurologist and infectious disease specialists
- CSF, respiratory (NP/OP), serum, and stool specimens should be also sent to CDC for surveillance testing*
- Consider additional pathogen-specific testing based on seasonality, exposures, and geography and clinical presentation

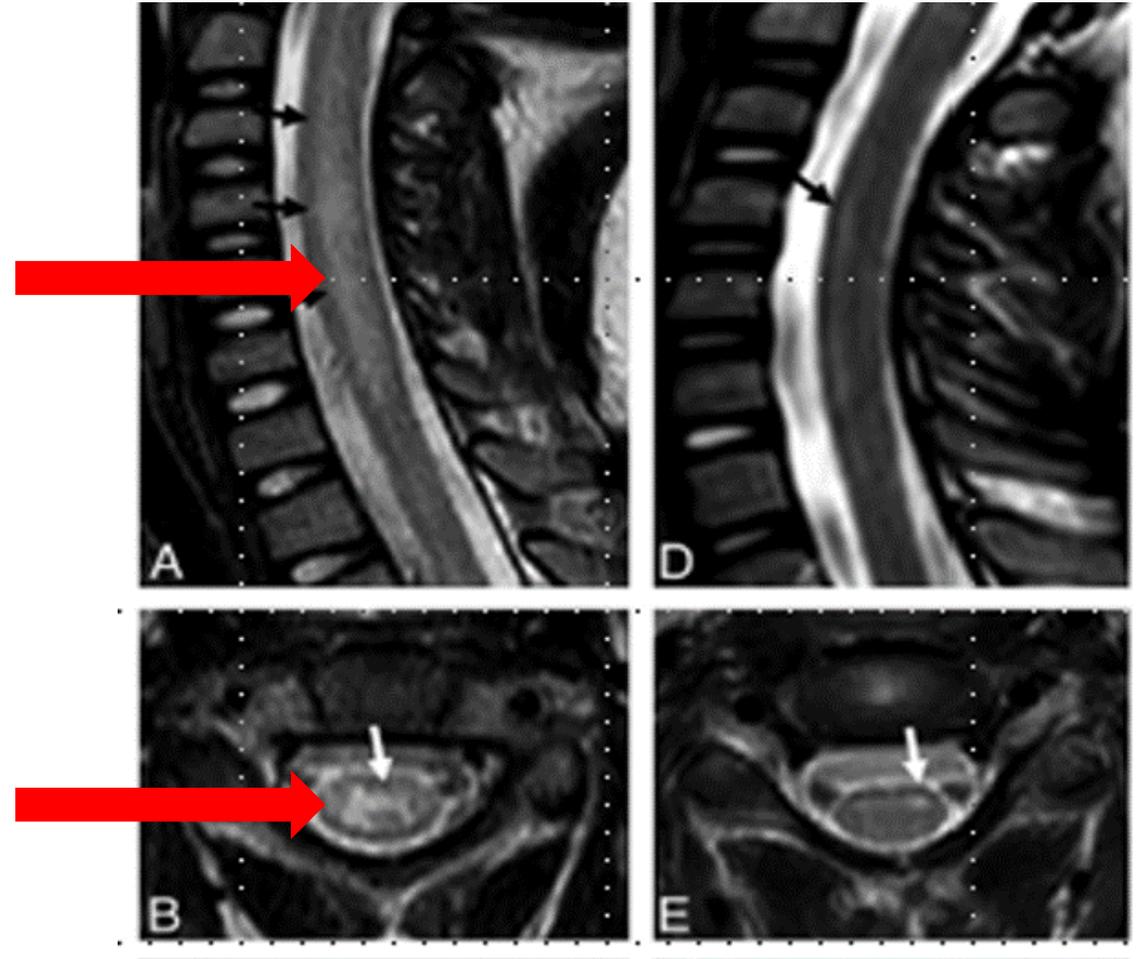
*Contact your health department to coordinate sending of specimens to CDC for testing: <https://www.cdc.gov/acute-flaccid-myelitis/hcp/contact-info.html>

MRI imaging

- Order MRI of the spine and brain with and without contrast
 - Use the highest tesla scanner available (ideally 3T)
- 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
 - Multiple levels of the spinal cord are often involved, consider imaging entire spinal cord
 - In patients with cranial nerve deficits, high cuts of brainstem or total brain MRI should be considered
 - Although lesions are predominantly grey matter, some patients with AFM may also have some white matter involvement

Characteristic MRI findings in AFM

- 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)



Clinical Management of AFM

What treatment can be considered for patients with AFM?

Hospitalize when AFM is suspected

- Assess the patient's ability to protect airway
 - Manage patient in hospital equipped with ventilator
- Consult with neurology and infectious disease experts to guide treatment and clinical management decisions
 - Siegel Rare Neuroimmune Association hosts a portal for clinicians to contact AFM experts with any question
 - To access the portal, visit: <https://wearesrna.org/living-with-myelitis/resources/afm-physician-support-portal/>
- Review the clinical considerations available on the CDC AFM website at:
 - <https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinical-management.html>
 - This document will be updated regularly as new evidence becomes available

Medical treatments for AFM

- Treatments commonly used for AFM in the acute phase include:
 - Intravenous immunoglobulin (IVIG)
 - Corticosteroids
 - 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 disease experts
 - Potential benefits of using corticosteroids for spinal cord edema or white matter involvement must be balanced by potential harm due to immunosuppression in the setting of a possible viral infection
 - There is no indication for the use of fluoxetine, antiviral, and/or other immunosuppressive agents for AFM

Reporting of AFM

How to report suspected AFM to public health department?

Disease Surveillance Process



Person with
cough and fever



Laboratory test



Case of illness

AFM Surveillance



Person with
limb weakness



Medical records
and MRI images



Case of AFM

Case definition for AFM

Confirmed case of AFM – Acute onset of limb weakness and magnetic resonance image (MRI) showing a spinal cord lesion largely restricted to gray matter *in a patient ≤21 years of age*

Confirmed case of AFM – Acute onset of focal limb weakness, AND an MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments.

Probable case of AFM – Acute onset of focal limb weakness, AND cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm³).

Confirmed case of AFM – Acute onset of flaccid limb weakness, AND an MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments.

Probable case of AFM – Acute onset of flaccid limb weakness, AND cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm³).

Confirmed case of AFM – Acute onset of flaccid limb weakness, AND an MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments* AND *absence of clear alternative diagnosis attributable to a nationally notifiable condition.*

Probable case of AFM – Acute onset of flaccid limb weakness, AND an MRI showing spinal cord lesion where gray matter involvement is present* but predominance cannot be determined AND absence of clear alternative diagnosis attributable to a nationally notifiable condition.

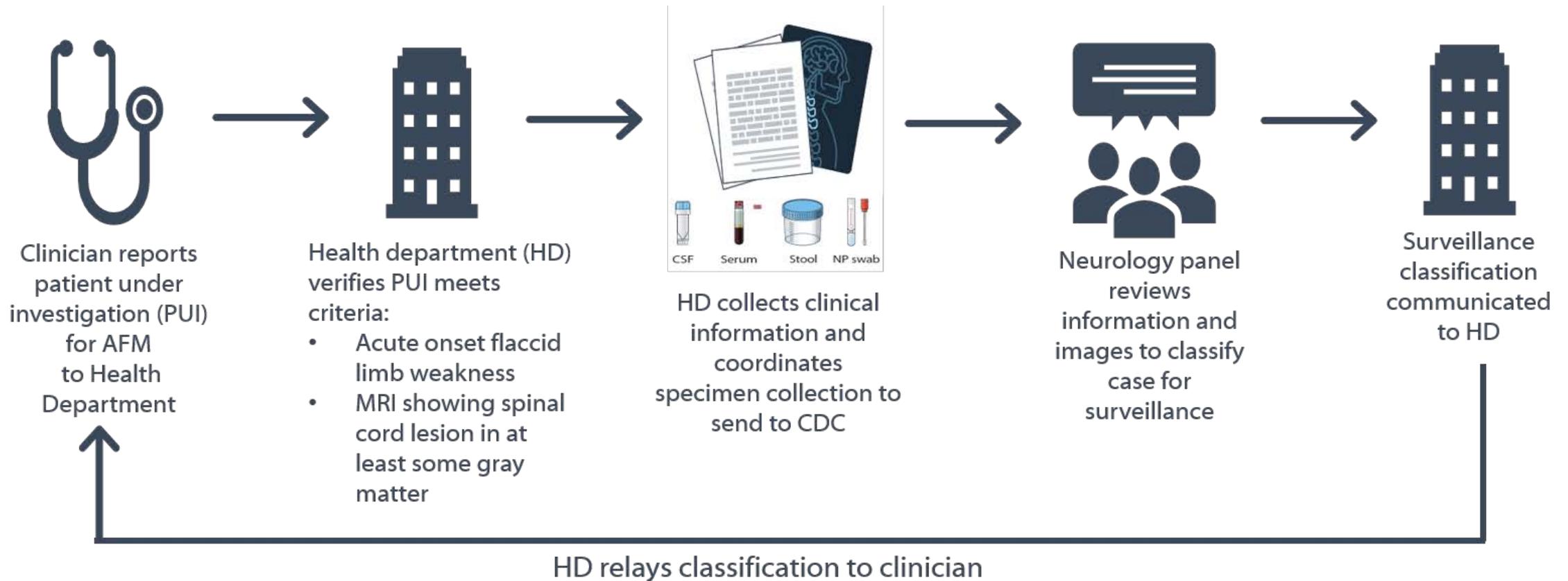
Suspect case of AFM - Acute onset of flaccid limb weakness, AND an MRI showing a spinal cord lesion in at least some gray matter and spanning one or more spinal segments* AND available information is insufficient to classify as confirmed or probable.

June 2019: CSTE adopted revisions to case definition



* Excluding persons with gray matter lesions in the spinal cord resulting from physician diagnosed malignancy, vascular disease, or anatomic abnormality.

AFM surveillance processes involve clinicians and health departments



Clinical diagnosis and public health surveillance have different purposes

Clinical Diagnosis

- Patient-level
- Used for individual clinical management decisions
- Time-sensitive
- Diagnosis based on full clinical presentation
- Aim for the most accurate diagnosis

Public Health Surveillance

- Population-level
- Use of standardized case definitions
- Measures disease burden and trends over time
- Delayed reporting and classification
- Balances sensitivity and specificity

Report suspected AFM patients who meet the AFM clinical criteria to public health

- Reporting of cases should not delay a patient's diagnosis and/or treatment and management plan
- A case classification by CDC is not meant to override a clinician's diagnosis of a patient's illness, or their treatment and rehabilitation plan
- Sharing information through reporting is vital for a better understanding of AFM and its pathogenesis to inform treatment and prevention strategies
- For more information on reporting, see CDC's webpage for clinicians and health departments:
<https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinicians-health-departments.html>

AFM Clinical Criteria for Reporting:

- Acute onset of flaccid limb weakness
- MRI showing a spinal cord lesion in at least some gray matter
 - (even if lab results are still pending)

Knowledge Check 2

Which is NOT a way to decide on AFM diagnosis?

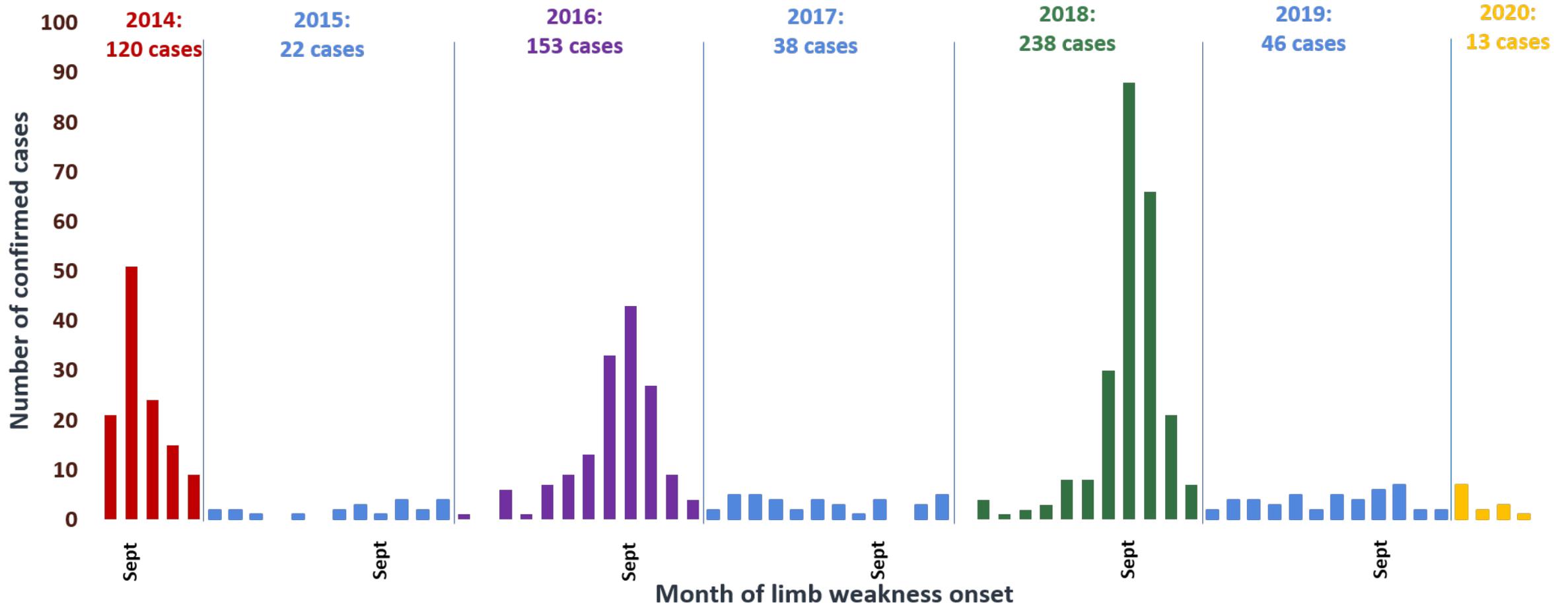
- a) Consult with a neurologist in your institution
- b) Consult experts via SRNA's AFM Physician Consult Portal
- c) Review information about AFM on the CDC website
- d) Wait for CDC to report back on the final case classification
- e) Search for publications about AFM in medical literature

- Answer: **d) Wait for CDC to report back on the final case classification**

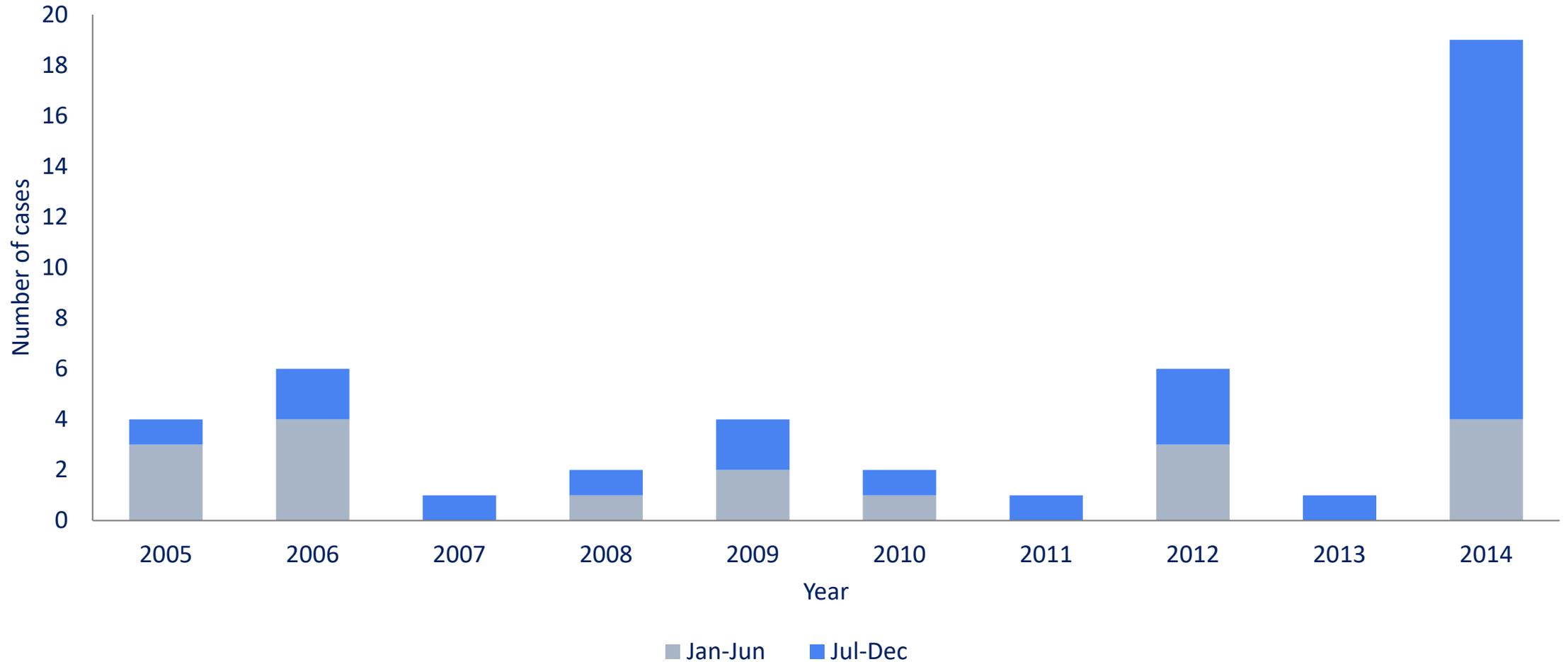
Epidemiology of AFM

National increase in AFM cases every 2 years since 2014

Number of confirmed reported AFM cases, Aug 2014 – June 2020 (n=630)

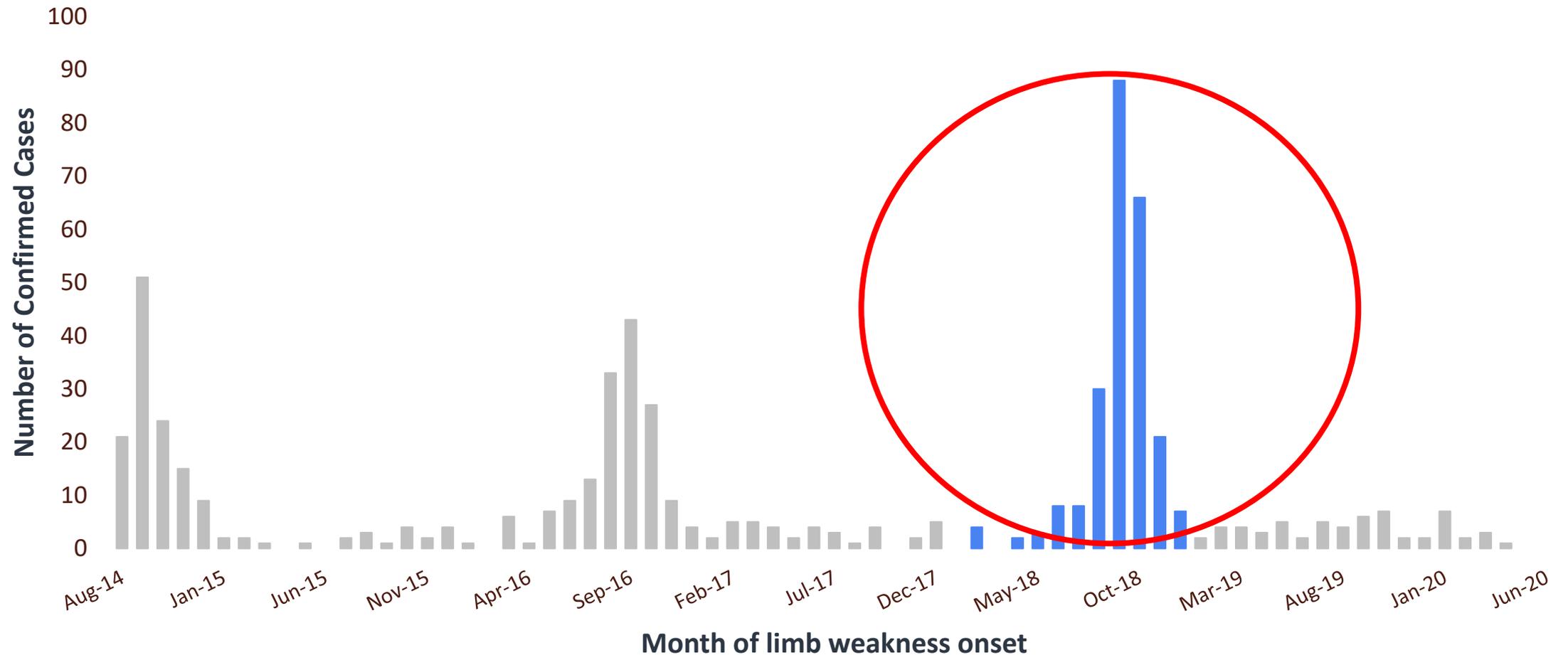


AFM cases, 2005–2014, 5 sites, United States

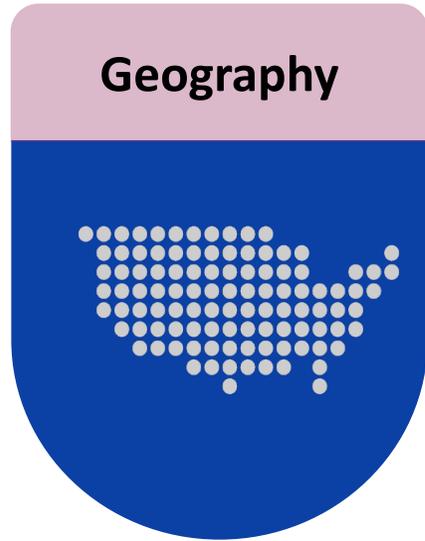


2018 was the most recent peak year for AFM

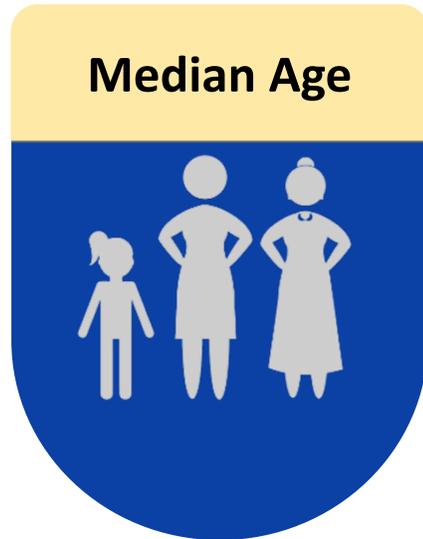
Confirmed reported AFM cases, January – December, 2018 (n=238)



Demographic characteristics of confirmed AFM cases, 2018



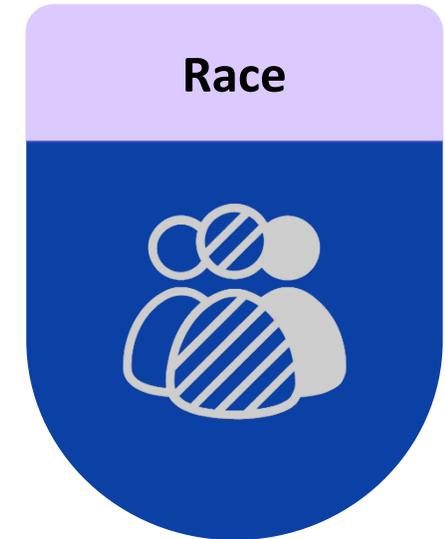
42 states



5.3 years
(IQR: 3.3—8.2)
94% <18 years

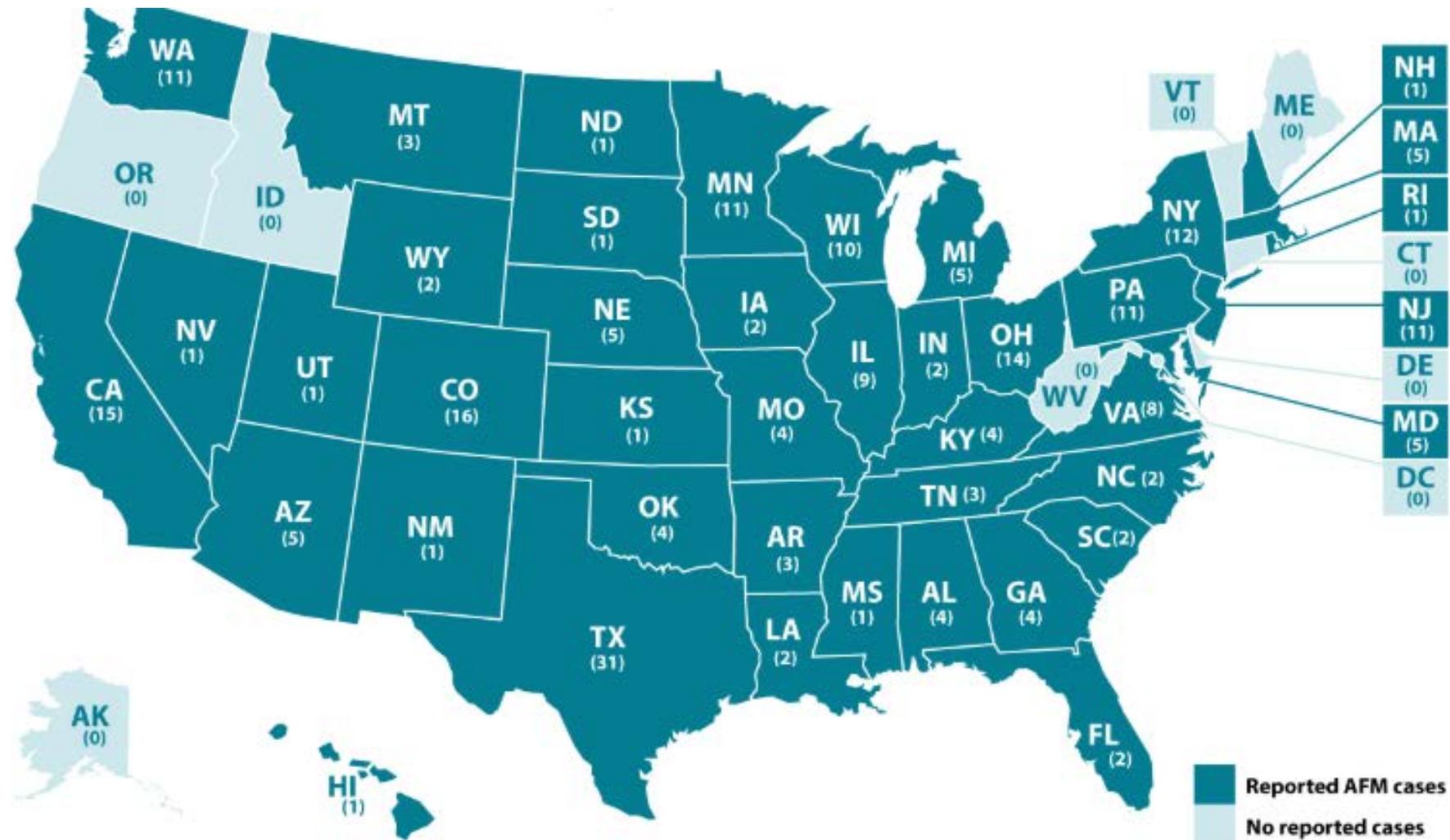


58% male



53% White
20% Hispanic
9% Black
3% Asian

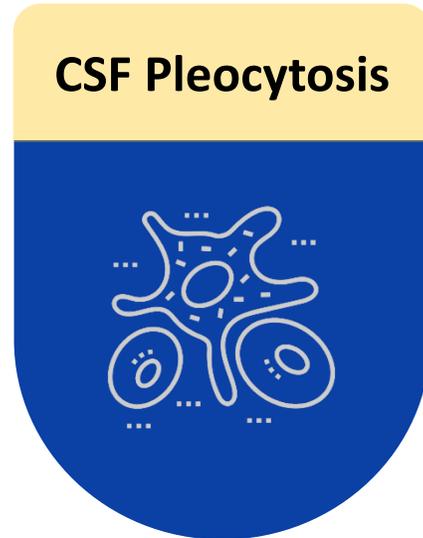
No geographic clustering of AFM among 238 cases in 42 states



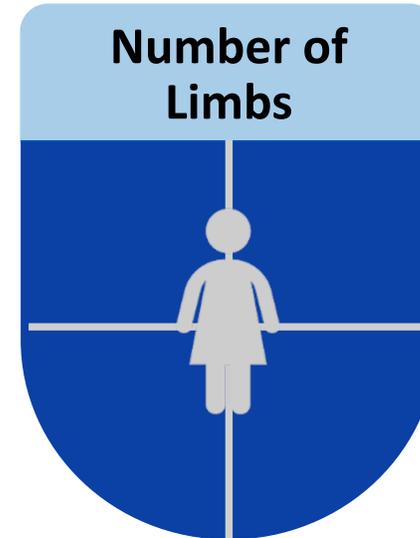
Clinical characteristics of confirmed AFM cases, 2018



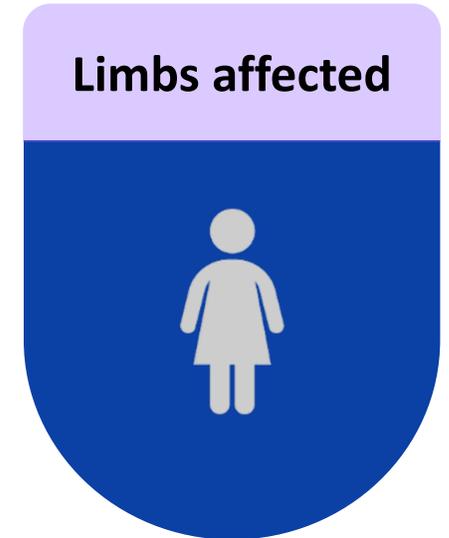
98%
(54% ICU)



87%
WBC count 94 cells/mm³
(IQR: 43–163)
Lymphocyte predominance

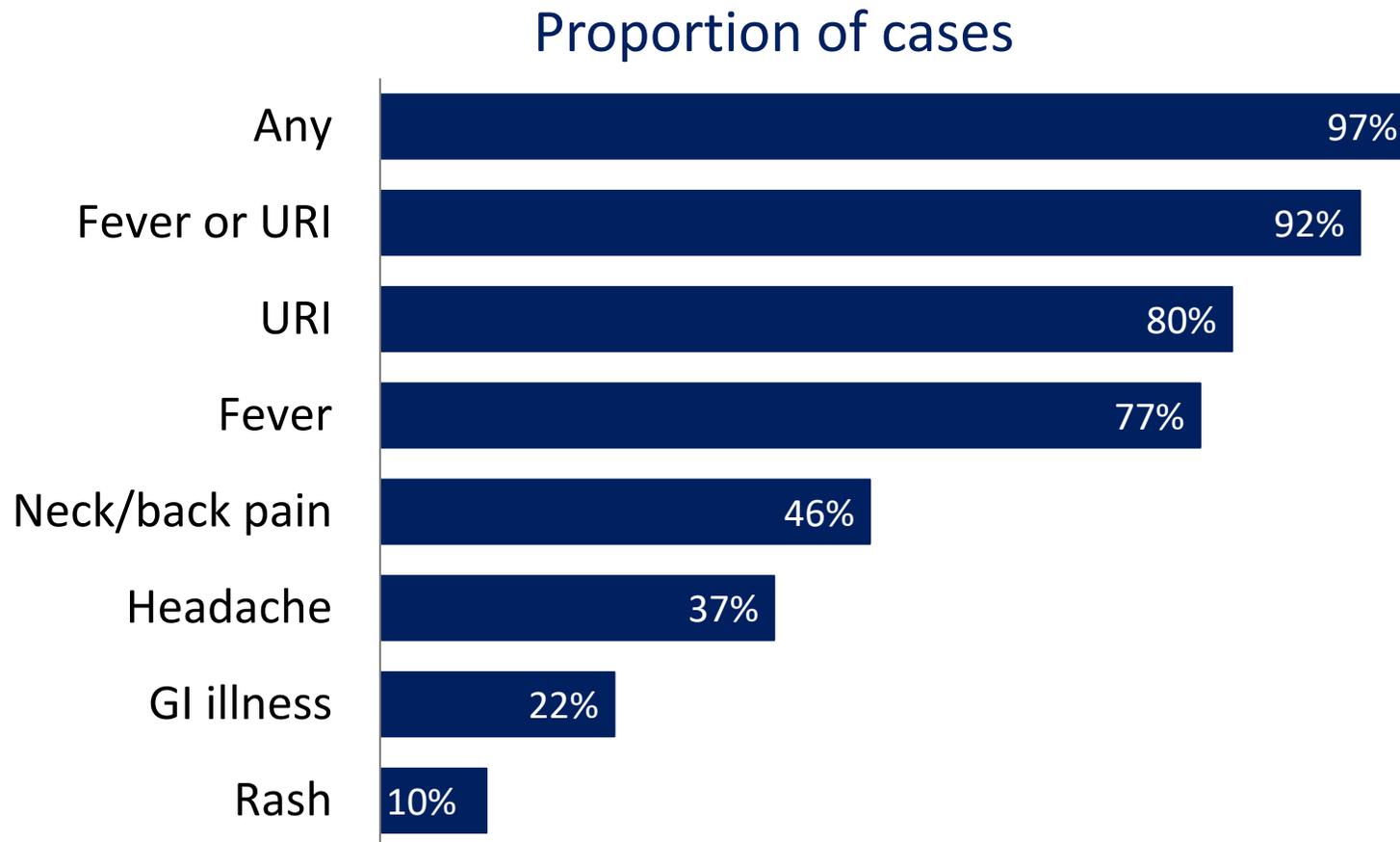


1 limb: 37%
2 limbs: 30%
3 limbs: 6%
4 limbs: 27%



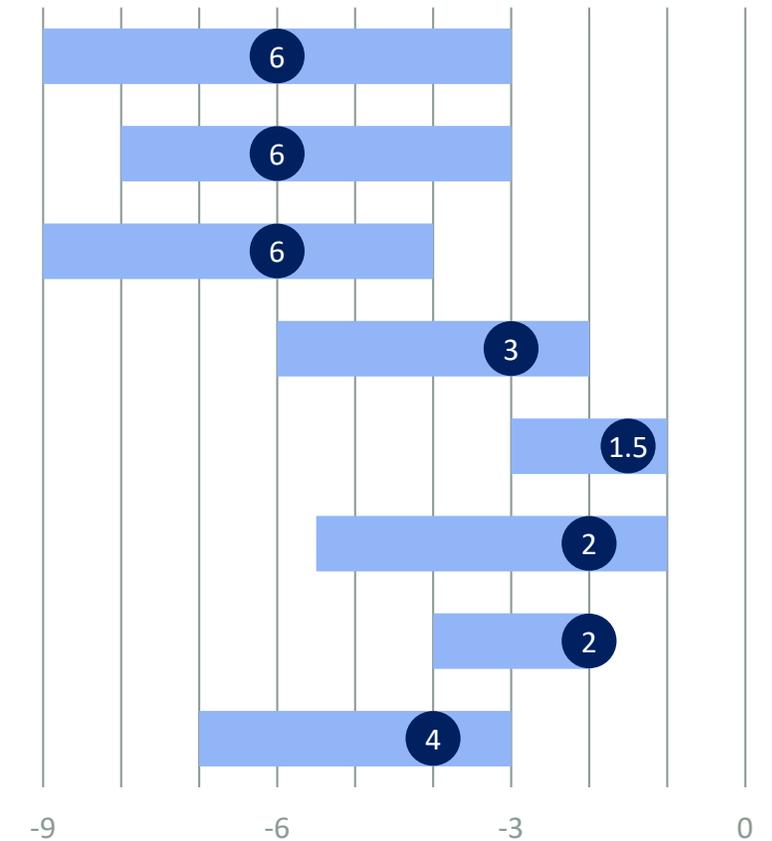
47% **upper** only
16% **lower** only

Symptoms consistent with a viral illness precede limb weakness



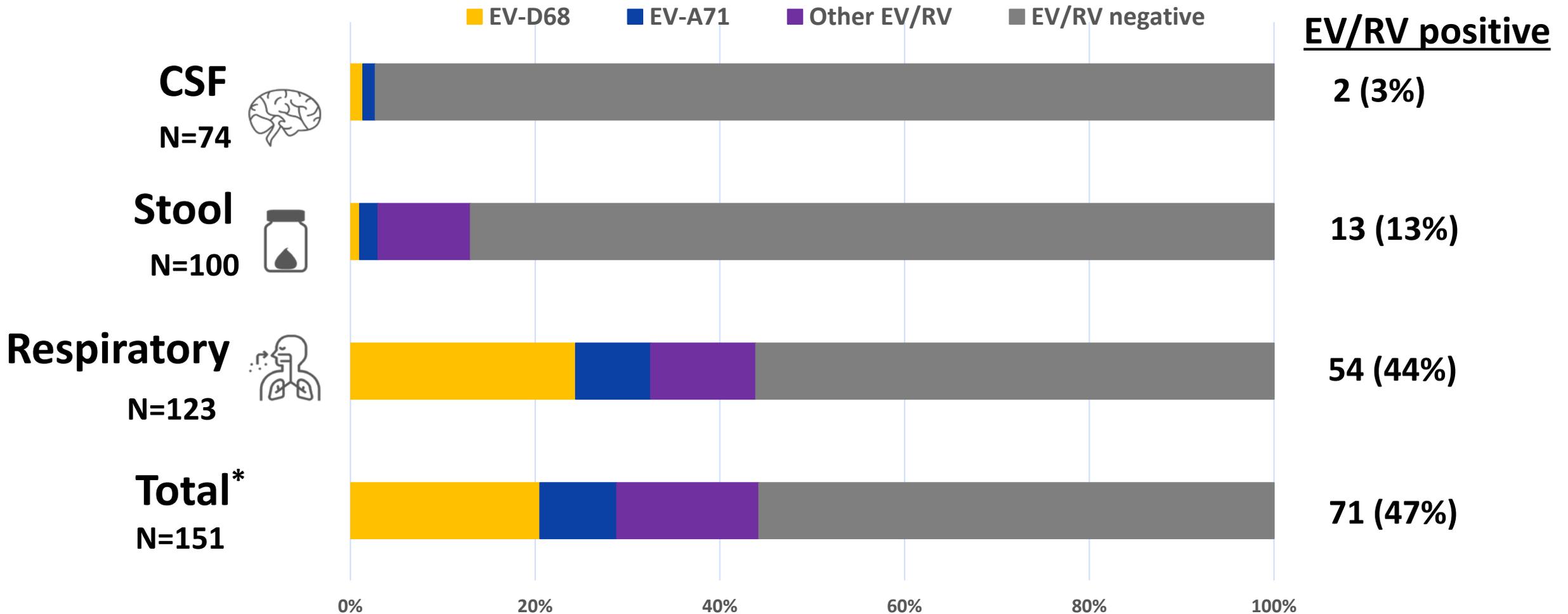
Days from symptom onset to limb weakness

Median (IQR)



AFM diagnostic testing remains low yield

CDC testing results, 2018



*Some patients had multiple positive specimens

Further evidence for role of enteroviruses in AFM

 AMERICAN SOCIETY FOR MICROBIOLOGY |  mBio®

RESEARCH ARTICLE
Clinical Science and Epidemiology

Antibodies to Enteroviruses in Cerebrospinal Fluid of Patients with Acute Flaccid Myelitis

Nischay Mishra,^a  Terry Fel Fan Ng,^b Rachel L. Marine,^b Komal Jain,^a James Ng,^a Riddhi Thakkar,^a Adrian Caciula,^a Adam Price,^a Joel A. Garcia,^a Jane C. Burns,^c Kiran T. Thakur,^d Kimbell L. Hetzler,^e Janell A. Routh,^b Jennifer L. Konopka-Anstadt,^b W. Allan Nix,^b Rafal Tokarz,^a Thomas Briese,^a M. Steven Oberste,^b W. Ian Lipkin^a

 nature medicine

LETTERS
<https://doi.org/10.1038/s41591-019-0613-1>

Pan-viral serology implicates enteroviruses in acute flaccid myelitis

Ryan D. Schubert ^{1,2}, Isobel A. Hawes^{1,2,18}, Prashanth S. Ramachandran^{1,2,18}, Akshaya Ramesh^{1,2,18}, Emily D. Crawford^{3,4}, John E. Pak³, Wesley Wu³, Carly K. Cheung³, Brian D. O'Donovan⁵, Cristina M. Tato³, Amy Lyden³, Michelle Tan³, Rene Sit³, Gavin A. Sowa⁶, Hannah A. Sample⁵,

- Both studies found that AFM cases had higher levels of enterovirus-specific antibodies in CSF compared with non-AFM controls
- Results are supportive of the leading hypothesis that enterovirus infection plays a key role in development of AFM

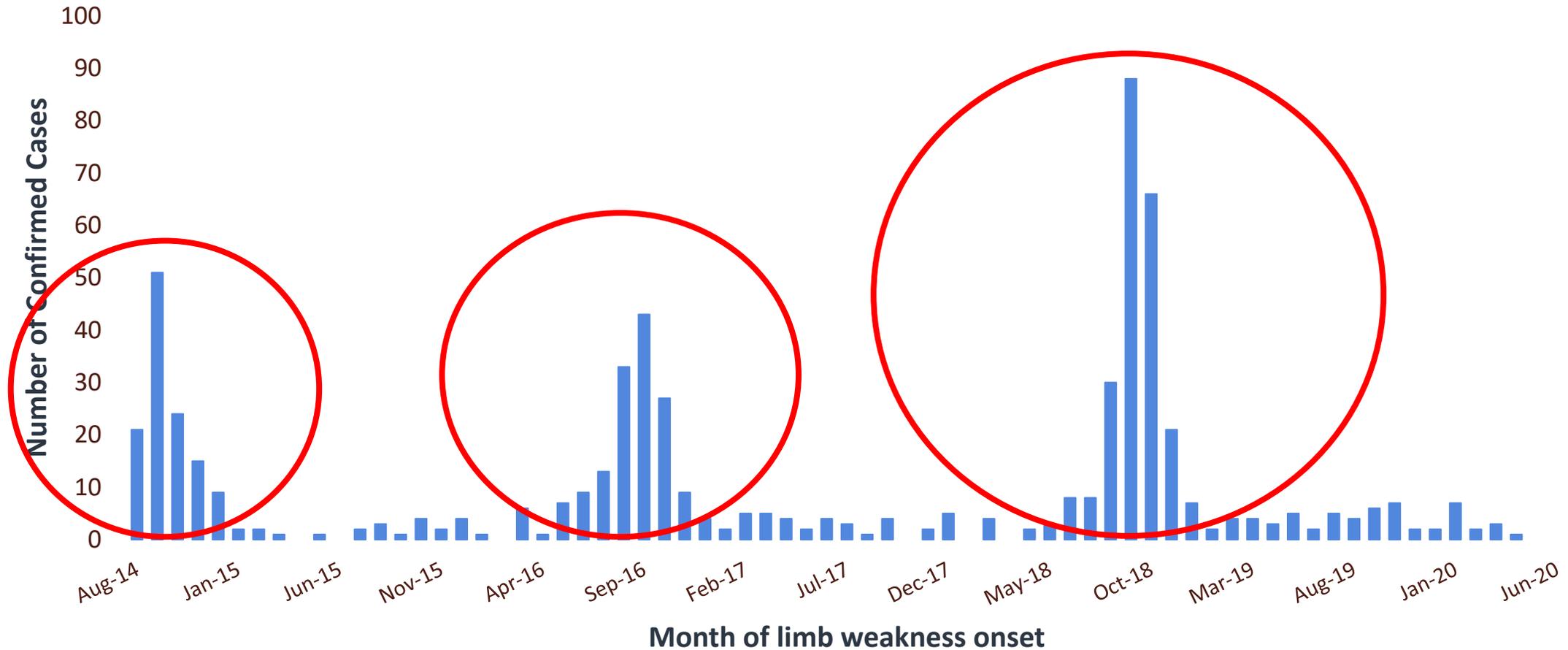
Knowledge Check 3

Outbreaks of AFM in the U.S. have been occurring during _____, starting in 2014.

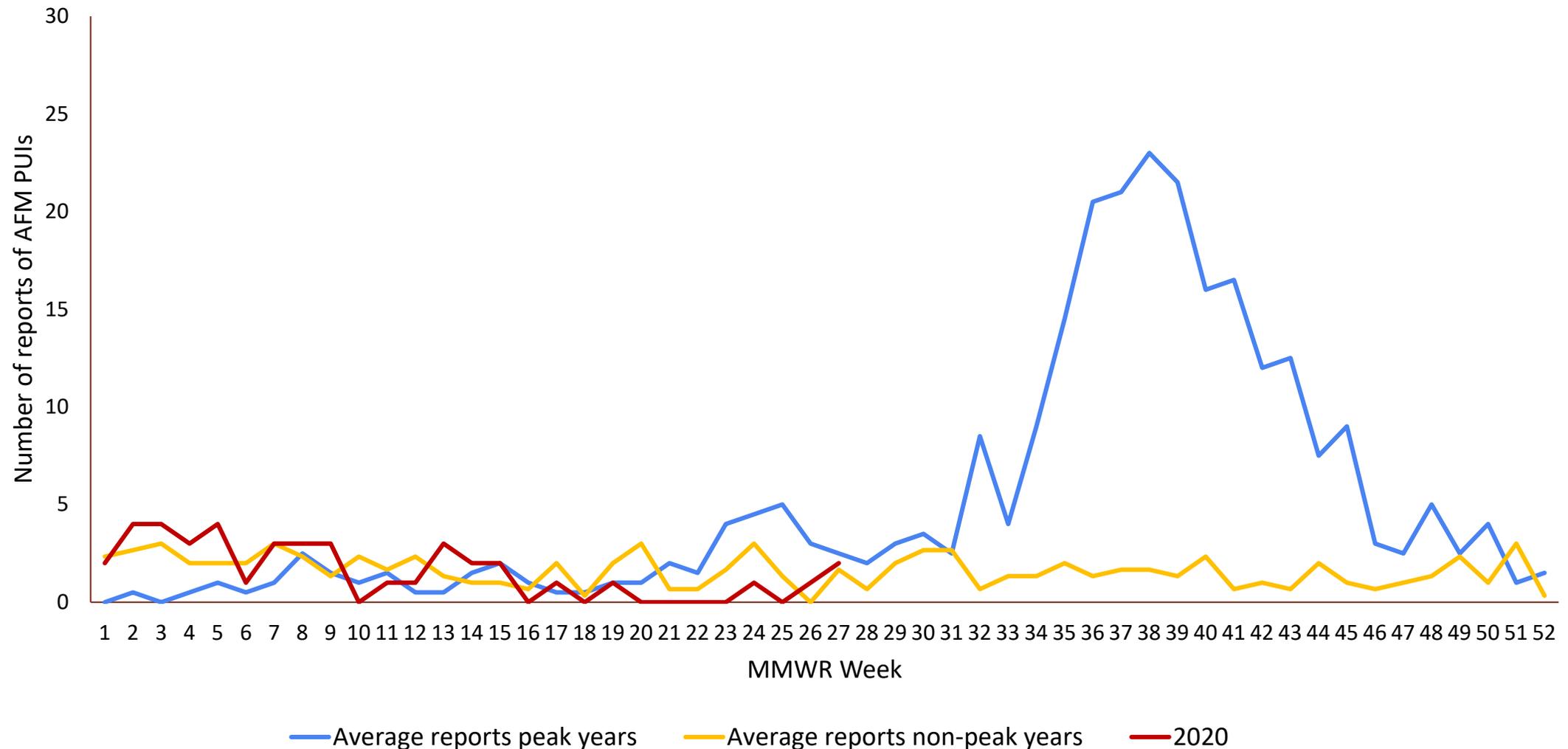
- a) Flu season, every year
- b) Holidays
- c) Every winter and spring
- d) Late summer through fall every other year

- Answer: **d) Late summer through fall every other year**

What can we expect for AFM in 2020?



Current number of suspect AFM cases reported to CDC is typical of both peak and non-peak years for this time period



Data current as of June 30, 2020.

Summary

Recognize, Hospitalize, Report

Roles, responsibilities, and scope of practice in addressing AFM

Healthcare professionals involved in recognizing, diagnosing, hospitalizing, and treating patients, as well as reporting cases to health departments



*Any clinician who suspects AFM should promptly report to their health department.

AFM patients can deteriorate quickly and rapidly progress to respiratory failure

- Most patients have a preceding febrile illness 1-2 weeks before acute onset of limb weakness
- Perform and document a thorough neurologic exam
- Hospitalize when AFM is suspected
- Assess the patient's ability to protect airway
- Manage patient in hospital equipped with ventilator
- Obtain specimens early to optimize yield for detecting a pathogen, including CSF through lumbar puncture
- Order MRI of the full spine and brain (sedation may be required)
- Consult with neurology and infectious disease experts to guide treatment and clinical management decisions

AFM Resources for Healthcare Professionals

Where to find most up-to-date information about AFM?

CDC AFM website

- <https://www.cdc.gov/acute-flaccid-myelitis/>
 - Clinician Job Aid
 - Clinical Presentation
 - Initial Evaluation and Diagnostic Studies
 - Clinical Management Considerations
 - Slide set Clinical Overview of AFM
 - FAQs from clinicians and health departments
 - Up-to-date surveillance data
 - AFM Vital Signs Report
 - 2019 AFM report: www.cdc.gov/vitalsigns/afm/
 - 2020 AFM report to come out on August 4 (MMWR, fact sheet for clinicians, webpage)



Resources for parents

- CDC Parent webpages
- AFM fact sheet
- AFM symptoms poster
- Stories from families affected by AFM
- AFM Parent Information Sessions
 - First occurred on June 25, more planned
- Email box for parent and public inquiries
 - AFMquestions@cdc.gov
- Working with patient advocates
 - Siegel Rare Neuroimmune Association
 - Acute Flaccid Myelitis Association

For Parents: Helping Children Who Have AFM

Acute flaccid myelitis (AFM) is a rare but serious condition. It causes arm or leg weakness, mostly in children. CDC believes that viruses, including enteroviruses, play a role in AFM. There is currently no proven way to treat or prevent AFM. [Learn more](#)

AFM can be devastating for patients and their families. CDC knows that families are facing uncertainties when it comes to their child's recovery from AFM. We are keeping these children front and center as we work with our partners to better understand AFM, research why some people get this condition, and develop ways to treat and prevent it.

We invite you to share questions you have by sending them to AFMquestions@cdc.gov.

ACUTE FLACCID MYELITIS (AFM) IN CHILDREN
A FACT SHEET FOR PARENTS

Acute flaccid myelitis (AFM) is an uncommon but serious neurologic condition that causes weakness in the arms or legs. If your child develops these symptoms, you should seek medical care for them right away.

What are the symptoms of AFM?
AFM affects a child's nervous system, specifically their spinal cord. It usually starts with sudden onset of limb weakness and loss of muscle tone and reflexes. Some may also experience:

- facial droop or weakness
- difficulty moving
- drooping eyelids
- difficulty with swallowing

Less common symptoms include tingling in the limbs. A child may also have weakness that requires them to breathe supportively.

Most children with AFM will have sudden onset of arm or leg weakness.

How is AFM diagnosed?

How to Spot Symptoms of Acute Flaccid Myelitis in Your Child.
Acute flaccid myelitis, or AFM, is an uncommon but serious condition that affects the nervous system.

Seek medical care right away if your child has any of these symptoms.

The Most Common Symptom of AFM
Sudden arm or leg weakness

Some People May Experience
Difficulty moving the eyes or drooping eyelids

The Nervous System
Brain
Spinal Cord
Nerves

Facial droop

Difficulty swallowing or slurred speech

Continuing education opportunities

- Claim CE credits for this webinar

CE Value	CE Type
0.100	CEU (other professionals)
1.000	CME (physicians)
1.000	CNE (nurses)
1.000	CPH (public health professionals)

- <https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinicians-health-departments/webinar-2020.html>

CDC Public Health Grand Rounds

- Date: July 21, 1:00 p.m. ET
- Topic: Acute Flaccid Myelitis: Answering Questions Through National Collaborations
- www.cdc.gov/grand-rounds
- CE credits will be available

Clinician questions

- Reporting: contact health department
 - State and Local AFM Contacts for Clinicians: <https://www.cdc.gov/acute-flaccid-myelitis/hcp/contact-info.html>
- Consultation on a suspected case with an AFM expert
 - SRNA portal for clinicians: <https://wearesrna.org/living-with-myelitis/resources/afm-physician-support-portal/>
- CDC
 - Urgent: CDC Emergency Operations Center 770-488-7100
 - Non-urgent: AFMinfo@cdc.gov

For more information

Visit www.cdc.gov/afm

Contact CDC AFM program at AFMinfo@cdc.gov

Contact other AFM specialists via the AFM Physician Consult and Support Portal:
<https://wearesrna.org/living-with-myelitis/resources/afm-physician-support-portal/>

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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