Acute Flaccid Myelitis

Update for 2019 MDHHS Communicable Disease Conference

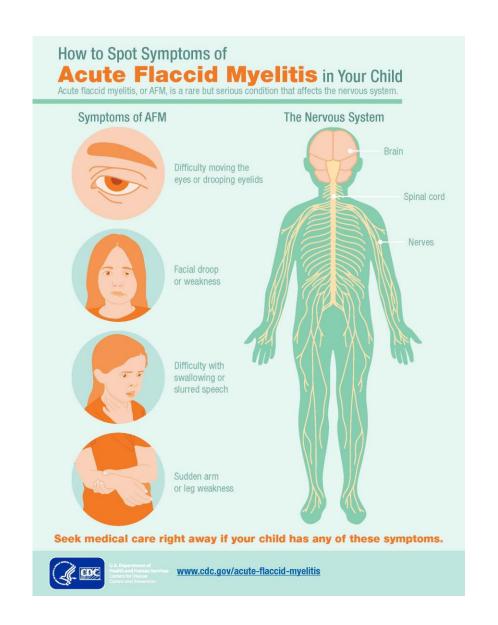
April 18, 2019

Nicole Parker-Strobe, MPH



What is AFM?

- A rare, serious condition affecting the nervous system, specifically the gray matter, causing muscles and reflexes to become weak
- CDC estimates that 1-2/1 million children in US will get AFM each year
- >90% of patients had a mild respiratory illness or fever prior to AFM symptoms



What is known from study of prior outbreaks?

- Prior to the 2018 outbreak there were two large national outbreaks
 - 2014
 - A retrospective cohort of 48 patients associated with hospital facilities found that AFM development may be a rare clinical manifestation after enterovirus D68 infection (Greninger et al, Lancet, 2015)
 - A cohort study of 12 outbreak cases in 2014 found that at 1 year cases were able to regain some function but weakness in affected limbs was persistent (Martin et al, Neurology, 2017)
 - 2016
 - Amongst a cluster of 10 cases reported in Washington from September November 2016, no common etiology of exposure was found (Bonwitt et al, MMWR Weekly, August 2017)
 - Enterovirus-A71 was detected in one patient and EV-D68 in two patients, one of whom also tested positive for adenovirus.
 - A review of 4 cases reported from an acute care facility in Maricopa County, AZ found that no single etiology or risk factor was associated with the confirmed cases (Iverson et al, MMWR Weekly, July 2017)

What is Causing AFM?

- Pathogenesis undetermined
 - Risk factors unknown
 - Predominantly a pediatric illness
- Seasonal trend, geographically dispersed
- Prodrome of fever/resp illness (90%) suggests infectious etiology
 - No consistent/single etiology identified in specimens from confirmed cases
 - Direct viral invasion of neural tissue?
 - Post-infectious syndrome?
 - Exploratory immunologic testing at CDC



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How AFM Cases are Reported & Investigated

- Required reportable condition in Michigan (Jan 2019)
- Providers with a suspect
 AFM case notify their LHD or MDHHS
- Complete the Patient Under Investigation Form and submit to MDHHS; include any preliminary testing results
- Forward clinical specimens such as stool, blood, respiratory, and spinal fluid to the Michigan Bureau of Laboratories

2019

REPORTABLE DISEASES IN MICHIGAN

A Guide for Physicians, Health Care Providers a

Report the following conditions to the Michigan Disease Surveillance System (MDSS) or local hea within 24 hours (unless otherwise noted) if the agent is identified by clinical or labor

Report the unusual occurrence, outbreak or epidemic of any disease or condition, including hed

Acute flaccid myelitis (1)
Anaplasma phagocytophilum (Anaplasmosis)
Arboviral encephalitides, neuro- and non-neuroinvasive:
Chikungunya, Eastern Equine, Jamestown Canyon, La Crosse,
Powassan, St. Louis, West Nile, Western Equine, Zika (6)

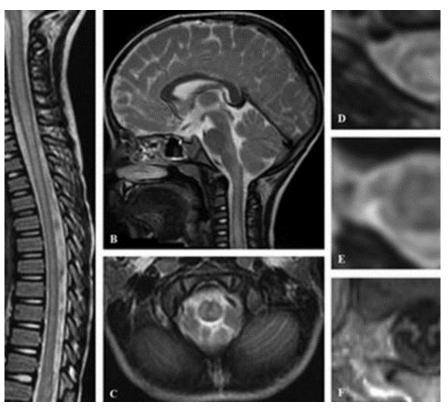
Klebsiella spp., Carbapenemase F Legionella species (Legionellosis) Leptospira species (Leptospirosis Listeria monocytogenes (Listerio Measles virus (Measles/Rubeola)

Specimens to collect and send to CDC for testing of Persons Under Investigation 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℃	Ship on dry ice

How AFM Cases are Reported & Investigated (cont'd)

- Send medical records including:
 - Consult notes
 - Lab reports
 - MRI reports of spinal cord and brain
- MRI image files are also needed
 - Multiple dates
 - Usually need to be requested through hospital radiology department
 - May be sent directly to MDHHS on diskette



<u>Clinical Infectious Diseases</u> 66(5) - October 2017

How AFM Cases are Classified



All patient records (de-identified at MDHHS) and specimens are sent to CDC



CDC has panel of neurology experts to classify AFM cases based on information provided

The process can take several weeks



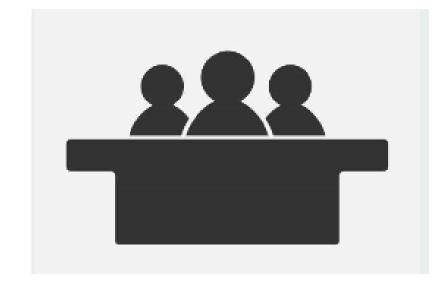
MDHHS receives classification from CDC

MDHHS notifies LHD

Public health shares classification with medical provider (no written report from CDC)



Confirmed cases are added to the CDC website



2018 AFM Case Definition

- 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/mm³)

^{*} 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.

2018 AFM Case Definition (cont'd)

Confirmed Case

- 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 Case
 - Clinically compatible case AND
 - Supportive laboratory evidence: CSF showing pleocytosis (white blood cell count >5 cells / mm³)

^{*} 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.

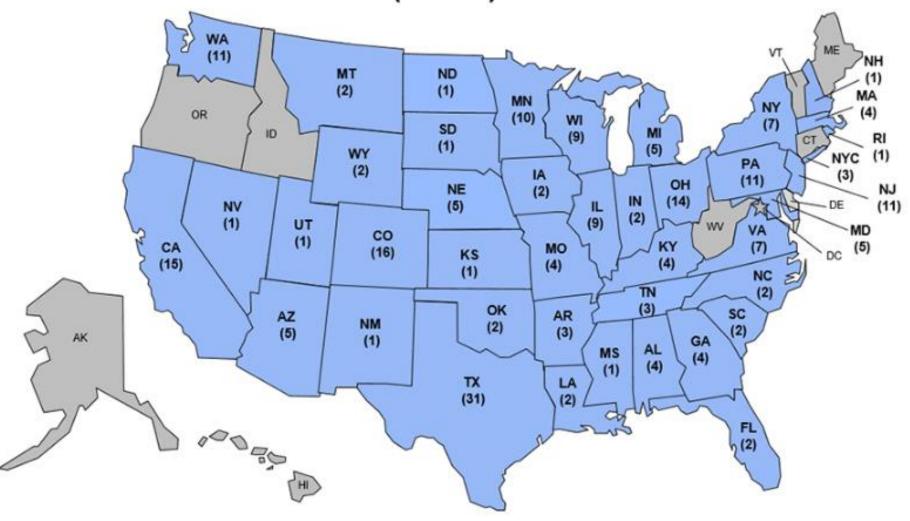
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AFM in the US 2014 – Present

- 2019 4 cases in 4 states*
- 2018 228 cases in 41 states*
- 2017 33 cases in 16 states
- 2016 149 cases in 39 states & DC
- 2015 22 cases in 17 states
- 2014 120 cases in 34 states, from Aug Dec

2018 AFM Outbreak

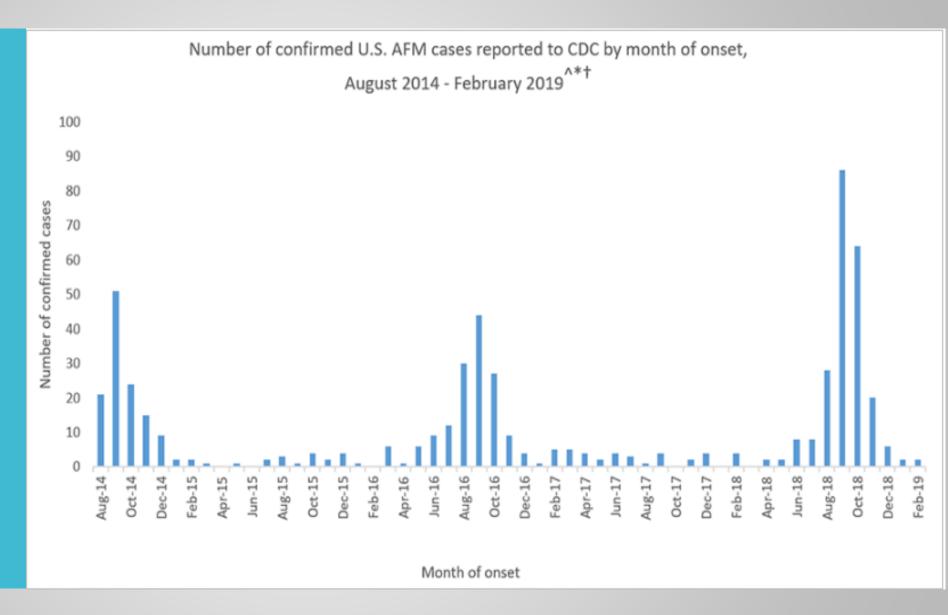
2018 confirmed cases of acute flaccid myelitis (AFM) by state (N=228)*



*Confirmed AFM cases as of March 29, 2019. Patients under investigation are still being classified, and the case counts are subject to change.

One of the confirmed cases is a foreign resident (based on the country of usual residence) and therefore not included in the state map.

AFM Cases 2014-March 29, 2019*

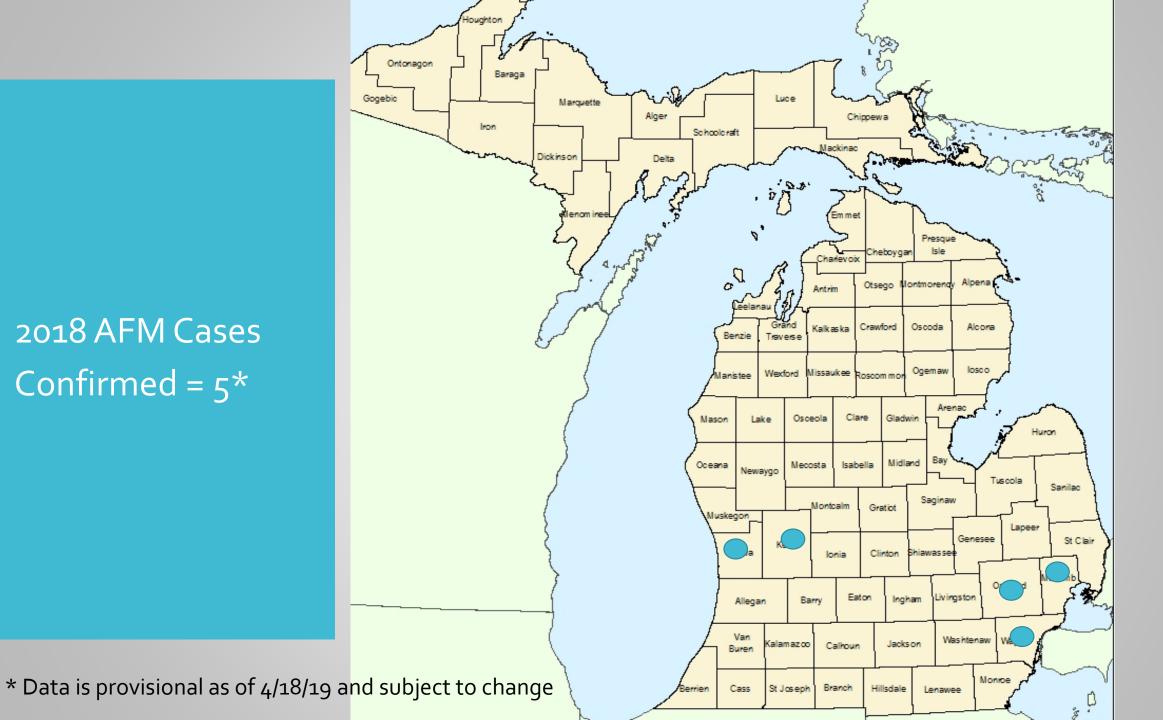


AFM in Michigan 2014-Present

- 2019 o confirmed cases to date*
- 2018 5 confirmed cases (preliminary), 1 probable*
- 2017 o cases
- 2016 1 confirmed, 1 probable
- 2015 1 confirmed
- 2014 4 confirmed



2018 AFM Cases Confirmed = 5*



Michigan AFM Cases – 2018 (preliminary)*

Confirmed Cases (N=5)

Median Age Group: 5-10 years (all children)

Gender: 60% M

Onset date range (limb weakness): 8/18 - 9/28

Cases with febrile/resp prodrome: 100%

Hospitalization rate: 100%

No deaths

Probable cases: 1 (adult)

Unclassified cases: 1 (pending CDC review)

Non-cases: 10



^{*} Data is provisional as of 4/18/19 and subject to change

2018 Michigan Enhanced Case Follow-up

For all AFM cases:

- Confirm medical and vaccine history
- Obtain hospital discharge summary once hospitalization completed
- Conduct 6o-day follow-up

For **2018** confirmed and probable AFM cases:

- Administer standardized functional questionnaire for 6 and 12 month follow-up
- Coordinate activities necessary to offer AFM cases standardized clinical evaluation by a healthcare provider

MDHHS staff will be conducting the enhanced follow-up with confirmed and probable cases from 2018

CDC: Clinical Considerations

- Acute Flaccid Myelitis: Interim Considerations for Clinical Management
 - Updated (Nov 2018) by national panel of experts
 - Summarizes experts' approaches to clinical treatment of AFM
 - https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinical-management.html#experts
- No proven treatment
 - No targeted therapies/interventions with enough evidence to endorse or discourage their use
- Sparse published evidence for treatment of AFM
 - Limited to case reports and case-series of patients with AFM
- Manage AFM patients in consultation with neurology and infectious disease experts

Resources for Clinicians and Public Health

Date Received: 10/25/2018 02:49 PM EDT

Sender: Michigan Health Alert Network

Subject: Increase in Reports of Acute Flaccid Myelitis--2018

Message:

Summary

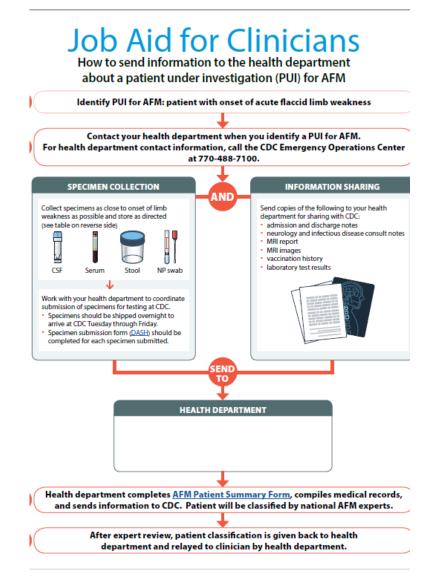
Nationally there has been an increase in reported acute flaccid myelitis (AFM) cases since August 2018. From January 1 through October 19, 2018, the Centers for Disease Control and Prevention (CDC) received 155 reports of patients under investigation for AFM in persons from 35 U.S. states; 62 AFM cases have been confirmed thus far. In Michigan, four individuals are being evaluated for AFM. Clinicians are encouraged to maintain vigilance for AFM among all age groups and to report patients with acute onset of flaccid limb weakness to the Michigan Department of Health and Human Services (MDHHS). Reporting of cases will help states and CDC monitor the occurrence of AFM and better understand factors associated with this illness.

Recommendations

- CASE REPORTING: Clinicians should send the following information about all patients that
 meet the clinical criterion for AFM (acute onset of flaccid limb weakness) to MDHHS:
 - Michigan AFM patient summary form
 (https://www.michigan.gov/documents/mdch/20150827_AFM_Patient_Summary_Form_MI_4_98628_7.pdf
 - o Admission and discharge notes

AFM Resources

- MDHHS Communicable Disease Division, Tel 517-335-8165; Fax 517-335-8263
- www.Michigan.gov/cdinfo
 - CDC test requisition form
 - Clinical management of AFM
 - CDC AFM fact sheet
 - Michigan AFM patient summery form
 - CDC AFM job aid for clinicians
 - AFM FAQ
 - AFM case determination SOP
- https://www.cdc.gov/acuteflaccid-myelitis/



AFM Public Notifications

First case of Acute Flaccid Myelitis confirmed in Michigan

FOR IMMEDIATE RELEASE: Dec. 5, 2018

CONTACT: Lynn Sutfin, 517-241-2112

LANSING, Mich. – The Michigan Department of Health and Human Services (MDHHS) was notified today by the Centers for Disease Control and Prevention (CDC) that Michigan has a confirmed case of acute flaccid myelitis (AFM). This marks the first confirmed case of AFM in Michigan in 2018. The confirmed case is a child from Wayne County.

Seven suspect cases of AFM in Michigan remain under investigation.

As of Nov. 30, the CDC had confirmed 134 cases of AFM in 33 states, mostly in children. Despite increases in cases across the country since 2014, the CDC estimates that less than one to two in a million children in the United States will get AFM annually.

AFM is a rare but serious condition affecting the nervous system and can cause the muscles and reflexes in the body to become weak. Most patients report having a mild respiratory illness or fever consistent with a viral infection before developing AFM.

Healthcare providers are asked to report all patients they suspect of having AFM to their local health department.

For more information, visit the MDHHS Communicable Disease Information and Resources website or CDC.gov/AFM.

AFM Public Notifications

Fir Acute Flaccid Myelitis confirmed in second Michigan

FOR IMMEDIATE RELEASE: Dec. 13, 2018

CONTACT: Lynn Sutfin, 517-241-2112

FOR LANSING, Mich. - The Michigan Department of Health and Human Services (MDHHS) has been notified by the Centers for Disease Control and Prevention (CDC) that Michigan has a confirmed a second case of acute flaccid myelitis (AFM) in 2018. The confirmed case is a

LAN; child from Oakland County.

notifi The state's first AFM case was confirmed Dec. 5 and involves a child in Wayne County. Nine confi suspect cases of AFM in Michigan remain under investigation.

Mich The CDC had confirmed 158 cases of AFM in 36 states, mostly in children. Despite increases in cases across the country since 2014, the CDC estimates that less than one to Seve two in a million children in the United States will get AFM annually.

As of and reflexes in the body to become weak. Most patients report having a mild respiratory Dest illness or fever consistent with a viral infection before developing AFM.

The cause or trigger for AFM is not yet known. To help protect yourself or your child from developing AFM, the CDC recommends:

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· Getting vaccinated against poliovirus, which is one of the viruses known to cause AFM. However, this vaccine does not protect against other viruses that may cause AFM.

 Protecting yourself from bites from mosquitos, which can carry West Nile Virus, another cause of AFM, by using mosquito repellents, staying indoors at dawn and dusk and removing standing or stagnant water near your home.

· Washing your hands often with soap and water and avoiding close contact with people who are sick.

Resc Healthcare providers are asked to report all patients they suspect of having AFM to their local health department.

AFM Public Notifications

Fir Acute Two additional Michigan children diagnosed with acute child flaccid myelitis Mic FOR IMME Four cases total have been confirmed by CDC

CONTACT: FOR IMMEDIATE RELEASE: Dec. 18, 2018

FOR LANSING, CONTACT: Lynn Sutfin, 517-241-2112

been notific LANSING, Mich. – The Michigan Department of Health and Human Services (MDHHS) has confirmed been notified by the Centers for Disease Control and Prevention (CDC) that two additional LAN child from (cases of acute flaccid myelitis (AFM) have been confirmed in Michigan for 2018. The

notifi The state's confirmed cases involve children in Ottawa and Macomb counties.

confi suspect ca. The state's first AFM case was confirmed Dec. 5 and involves a child in Wayne County. A Mich The CDC heecond case was confirmed in an Oakland County child on Dec. 12. Five suspect cases of increases i AFM in Michigan remain under investigation, while one case was ruled not to be AFM by the

Seve two in a mil CDC. The four confirmed AFM cases had onsets of illness between August and October.

As of AFM is a reThe CDC had confirmed 165 cases of AFM in 36 states, mostly in children. Despite and reflexe increases in cases across the country since 2014, the CDC estimates that less than one to Dest illness or fetwo in a million children in the United States will get AFM annually.

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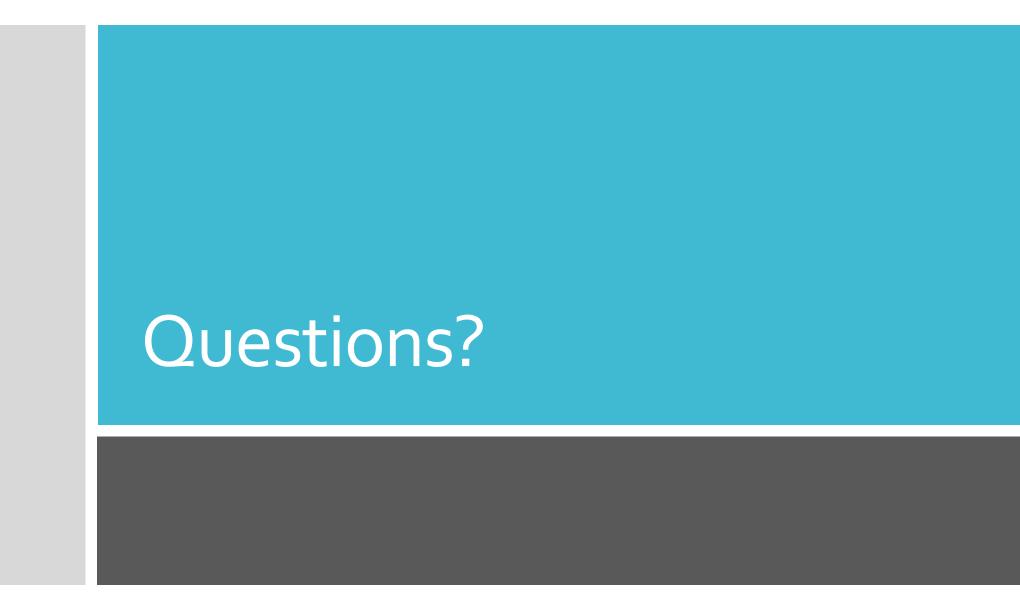
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References

- Bonwitt et al, Acute Flaccid Myelitis Among Children Washington, September – November 2016, MMWR Weekly, August 2017, 66(31);826–829.
 https://www.cdc.gov/mmwr/volumes/66/wr/mm6631a2.htm
- Greninger et al, A novel outbreak enterovirus D68 strain associated with acute flaccid myelitis cases in USA (2012-2014): A retrospective study, Lancet Infect Dis. 2015 Jun; 15(6): 671–682. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6027625/
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- Martin et al, Outcomes of Colorado Children with acute flaccid myelitis at 1 year, Neurology July 11, 2017; 89 (2). https://n.neurology.org/content/89/2/129