Acute Flaccid Myelitis

Andrew M. White, MD, PhD
Chief, Pediatric Neurology
Denver Health Medical Center

Case Report – J.N.

• 6 year old previously healthy female
• Presents with
  – Sore throat
  – Neck, left shoulder weakness
  – Left arm weakness and finger paresthesias
• Dx’d with strep pharyngitis, myalgias
• Arm pain and paresthesias improved over next several days
• Arm weakness was stable, non-progressive, more proximal than distal

Case Report – J.N.

• Physical exam
  – Normal VS
  – TTP in L upper arm and neck
  – CNs intact
  – Right arm strength – normal
  – Left upper extremity motor
    • 4/5 for finger flexors, extensors
    • 1/5 for wrist flexion/extension
    • 0/5 for elbow
Case Report – J.N.

- Left upper extremity sensation
  - Decreased in left forearm and upper arm (circumferentially)
- Reflexes 1+ in LUE, 2+ otherwise
- Normal muscle tone/bulk
- No problems in b/l lower extremities.
- Normal coordination on right
- Normal gait

Case Report – J.N.

- Imaging
  - Normal radiographs of shoulder, humerus, elbow
  - MRI brain/total spine
    - Incidental finding of closed lip schizencephaly and polymicrogyria b/l, absent septum pallucidum
    - Spine was normal (non-contrast)

MRI Showing R Schizencephaly
Case Report – J.N.

• EEG was performed to r/o prolonged Todd’s
  – Normal

• Shoulder MRI
  – asymmetric increase in signal on fluid sensitive
    sequences diffusely within the supraspinatus and
    infraspinatus musculature on the left side,
    consistent with edema
• F/U dedicated contrast enhanced MRI of C-spine
  – showed subtle linear high T2 signal within the left
    side of the ventral cord from C2 to C6 as well as
    ventral nerve root enhancement from C4-C7

Left STIR imaging of Shoulder
Coronal STIR imaging of bilateral shoulders showing slight infraspinatus and supraspinatus signal increase

Linear signal hyperintensity seen on T2 imaging

Case Report – J.N.

- EMG
  - Neural stimulation at Erb’s point along with the proximal medial upper arm was performed day #9 or less from the day of maximal neurological weakness
  - These stimulations resulted in no appreciated movement or palpable contraction of the deltoid or biceps musculature, a weak finger flexor response, and an absent CMAP recording over the biceps brachii indicating lower motor neuron involvement.
  - The results were consistent with either a localized alpha motor neuron cell injury, motor axon degeneration within the brachial plexus, or less likely, due to a complete conduction block.
Case Report – J.N.

• Film Array Respiratory Panel (BioFire Diagnostics, Inc)
  – Positive for Rhinovirus/Enterovirus
  – Sent to CDC for typing
  • Human rhinovirus 84B

Definitions

• Acute Flaccid Paralysis (AFP)
  – Sudden (acute) weakness in the arm(s) or leg(s), along with loss of muscle tone and decreased or absent reflexes. In some cases, there is pain or there can be an impact on the nerves controlling the head and neck, causing facial weakness, drooping of the eyelids, and difficulty swallowing, speaking, or moving the eyes.

• Acute Flaccid Myelitis (AFM)
  – A disease involving the spinal cord (specifically anterior horn cells), with symptoms of acute flaccid paralysis.
  – Coined in 2014 to describe patients with sudden onset limb weakness of unknown cause
  – Identical in clinical presentation to polio

Definitions

• CDC case definition (2014)
  – Presenting after 8/1/2014
  – Confirmed
    • Weakness and MRI evidence of predominantly gray matter lesion(s) spanning one or more spinal cord segments
  – Probable
    • Acute focal limb weakness and CSF pleocytosis (>5) WHO definition states that age < 15 yo

Council of State and territorial Epidemiologists. Standardized case definition for acute flaccid myelitis; centers for disease control and prevention, 2015.
Evolution of Case Definition

- Confirmed case of AFM:
  - Acute onset of focal limb weakness, AND
  - MRI showing a spinal cord lesion largely restricted to gray matter and sparing one or more spinal segments.
  - In a patient ≤21 years of age.

- Probable case of AFM:
  - Acute onset of focal limb weakness, AND
  - Cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm$^3$).

- Confirmed case of AFM:
  - Onset of acute limb weakness, AND
  - MRI showing a spinal cord lesion largely restricted to gray matter, AND
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  - In a patient ≤21 years of age.

Changed "focal" to "flaccid" and added "for consistency, review and final case classification will be done by experts in national AFM surveillance, similar to the review required for final classification of paralytic polio cases".

Polio Epidemiology

- Average cases of paralytic polio (1951-54)
  - 16,316/year

- Average deaths from polio (1951-54)
  - 1879/year

Epidemiology of AFM

- Reemerged in 2012; 3 pts. In CA
  - Originally associated with polio virus

- From 6/2012 – 6/2014, 23 cases reported

- 12 in Colorado 8/2014 – 10/2014

- 120 patients from 34 states presented between August and December, 2014
  - CA, CO, MA, PA, and UT with >5 cases

- CDC Surveillance established 2015
Epidemiology

- Current incidence is less than 1 in 2 million children
- Increases every two years
- Often preceded by respiratory or febrile illness
- Onset usually August through October
- Over 90% are children
- 46 states and DC
- 60% male; avg. age – 6.3 yo

https://www.cdc.gov/acute-flaccid-myelitis/afm-surveillance.html

2018 confirmed cases of acute flaccid myelitis (AFM) by state (N=232)*

AFM Confirmed U.S. Cases

https://www.cdc.gov/acute-flaccid-myelitis/afm-cases.html accessed 6/30/19
U.S. Epidemiology

- 8/2014 to 12/2014 – 120 cases
- 2015 – 22 cases in 17 states
- 2016 – 149 cases in 39 states
- 2017 – 35 cases in 16 states
- 2018 – 232 cases in 40 states
- Total of 430 cases from 8/14 – 11/18
- 2019 – 9 cases so far as of 6/30/19

Epidemiology

- Worldwide
  - Canada
  - India
  - Wales
  - Scotland
  - France
  - Sweden
  - Norway
  - Spain
  - Japan
  - Ethiopia
  - Germany
  - Holland
  - Argentina
  - Pakistan
Epidemiology

AFM Symptomatology

- Sudden (hours-few days) onset of arm/leg weakness and loss of muscle tone/reflexes
- Can also include
  - Facial droop
  - Oculomotor difficulties
  - Ptosis
  - Dysarthria/dysphagia
  - Pain in affected limb
  - Hoarse or weak cry
- Can include dysuria and dyspnea
- Rarely with sensory deficits
- Preceding illness 1-2 weeks prior to symptoms

CDC Handout
AFM Diagnosis

- Difficult diagnosis
- Made with MRI (brain and spinal cord, with and without contrast)
- EMG can help
- CSF analysis
- Respiratory, stool cultures should also be collected
- Differential includes
  - Transverse myelitis
  - Guillain-Barre
  - Toxic neuropathy
  - Muscle disorder

Neurologic Condition Causing Acute Flaccid Paralysis

- Acute Myelopathy
  - TM
  - Cord compression
- Anterior Horn Cell
  - Poliomyelitis
  - WIPPP
  - Nonpoliomyelitis
  - Other viruses
- Polyradiculopathy
  - GBS
- Peripheral neuropathy
  - Infectious
  - Diphtheria, Lyme, etc...
  - Ingestion related
  - Lead, poisonous plants
- NM Junction
  - MG
  - Botulism
  - Tetanus
  - Animal toxin
  - Organophosphate
- Muscle disorders
  - Polymyositis
  - Myositis
  - Hypokalemic periodic paralysis
  - Critical illness weakness

Differential Diagnosis of AFM

<table>
<thead>
<tr>
<th>AFM</th>
<th>Transverse Myelitis</th>
<th>AIDP</th>
<th>ADEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preceding illness</td>
<td>URI, GI, 7 days prior</td>
<td>URI, GI are common</td>
<td>URI, vaccine</td>
</tr>
<tr>
<td>Associated symptoms</td>
<td>Fever, meningeval signs, back pain</td>
<td>Dysesthesis, Paresthesia, Back pain</td>
<td>Leg pain, unsteady gait</td>
</tr>
<tr>
<td>Progression</td>
<td>Hours to days</td>
<td>Hours to days</td>
<td>Ascending weakness</td>
</tr>
</tbody>
</table>
| Distribution | Asym, U.E.H.E. | Sym or asy 
  | | Symmetric | Asymmetric |
| Tone | Flaccid | Flaccid – Spastic | Flaccid |
| DTR's | Decreased | Decreased | Increased |
| Sensory | Decreased | Common, Level | Common |
| Autonomic | Bowel/bladder | Bowel, Bladder | CV instability |
| CN deficit | Common | Common | Possibly |
| Muscles | Proximal | Variable | Variable |
Characteristic Findings

- US 2012-2015
- US 2014-2018
- Japan 8-12/2015
- US 2018

Clinical characteristics of Cases 2012-2015

- Composed of CDC, CDPH, CHCO, PCH (Utah) studies
- 61% male
- Average age – 8 yo
- Pre-existing conditions (Asthma/Immunocompromised) - 21%
- Prodromal illness (fever, URI, GI) – 89%
- Neurological Illness
  - Headache – 50%
  - Stiff neck – 42%
  - Pain – 13%

Clinical characteristics of Cases 2012-2015

- Neurological Deficits
  - Limb weakness – 98.5%
    - Upper extremities – 75%
    - Lower extremities – 62%
    - Asymmetric – 49%
  - Sensory involvement – 25%
  - Hyporeflexia – 81%
  - Cranial Nerve dysfunction – 30%
  - Bowel/bladder dysfunction – 39%
Laboratory Findings (2012-2015)

- CSF pleocytosis — 78%
  - Up to 888 WBC
- Elevated CSF protein — 48%
- Virus found in CSF — 1%
- EV-D68 in respiratory specimen — 21%
- Non-D68 rhino/enterovirus in respiratory specimen — 18%

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<table>
<thead>
<tr>
<th>Spectrum source</th>
<th>No. with specimens available (N of 256)</th>
<th>No. (%) positive</th>
<th>Positive test results (N of 101)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF</td>
<td>74 (29)</td>
<td>27 (36)</td>
<td>EV-D68 (1)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>143 (56)</td>
<td>56 (39)</td>
<td>EV-D68 (19)</td>
</tr>
<tr>
<td>Other</td>
<td>156 (61)</td>
<td>39 (25)</td>
<td>EV-D68 (2)</td>
</tr>
</tbody>
</table>

Spectrum source: CSF = cerebrospinal fluid; RES = respiratory. [https://www.cdc.gov/mmwr/volumes/68/wr/mm6827e1.htm?s_cid=mm6827e1_w#F1_down](https://www.cdc.gov/mmwr/volumes/68/wr/mm6827e1.htm?s_cid=mm6827e1_w#F1_down) accessed 7/10/19

MRI imaging

- Use 3 Tesla if possible
- Imaging may be normal in first 72 hours
  - Repeat if indicated
- Axial/Sagittal images are best
- Image entire spine
- With cranial nerve lesions, image brainstem

- T2 gray matter lesions spanning multiple vertebral levels on spinal cord MRI – 94%
- Nerve root enhancement on MRI – 30%
- Brainstem lesion on MRI – 38%
- Supratentorial lesions on MRI – 16%
EMG Findings (2012-2015)

- All patients had motor findings on affected limb
- No tested patients had sensory findings on affected limb
AFM Diagnostic Testing 8/14 – 11/18

• CSF had EV-D68, EV-A71 and Cox A16 (4 cases)
• Upper respiratory specimen (49% in 2018)
  – 20-30% EV-D68; 10% EV-A71
  – 1/3rd with other viruses
  – 1/3rd with no pathogen
• Stool (14% in 2018)
  – EV-A71 (1), EV-D68(1), Echo (1), Coxsackie (3), Parecho (1), Rhino (1)
• All stool negative for poliovirus

Additional Characteristics for AFM (2018)

• 96% hospitalized
  – 58% in ICU
• 81% CSF pleocytosis
  – Median cell count – 104
  – Lymphocytic predominance
• No deaths in 2018 (but 1 in 2017)
• Days from illness to limb weakness
  – Febrile – 2
  – GI – 2.5
  – Respiratory - 5

| Characteristic | Confirmed (N = 205) | Probable (N = 30) | P-value
greater 0.1 | P-value
greater 0.1 |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age yrs (IQR)</td>
<td>5.0 (3.0-8.8, 3.0-8.8)</td>
<td>2.9 (2.0-10.0, 2.0-10.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Male</td>
<td>140/205 (68)</td>
<td>14/30 (47)</td>
<td>0.001</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>96/205 (47)</td>
<td>10/30 (33)</td>
<td>0.46</td>
</tr>
<tr>
<td>Black or African-American</td>
<td>12/205 (6)</td>
<td>5/30 (17)</td>
<td>0.055</td>
</tr>
<tr>
<td>Other Hispanic/Other-White</td>
<td>1/205 (0.5)</td>
<td>0/30 (0)</td>
<td>0.46</td>
</tr>
<tr>
<td>White</td>
<td>142/205 (69)</td>
<td>14/30 (47)</td>
<td>1.00</td>
</tr>
<tr>
<td>Multiracial</td>
<td>9/205 (4)</td>
<td>1/30 (3)</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Abbreviations: AFM = acute flaccid paralysis; IQR = interquartile range; MRI = magnetic resonance imaging.
*5 cases possibly associated with confirmatory pathogen.

https://www.cdc.gov/mmwr/volumes/68/wr/mm6827e1.htm#F1_down
Organisms Recovered

<table>
<thead>
<tr>
<th>Organisms Recovered</th>
<th>CSF</th>
<th>Nasal</th>
<th>Stool</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>325</td>
<td>319</td>
<td>318</td>
<td>962</td>
</tr>
<tr>
<td>Samples tested</td>
<td>421</td>
<td>421</td>
<td>421</td>
<td>1263</td>
</tr>
</tbody>
</table>

**Notes:**
- CSF: Cerebrospinal fluid
- Nasal: Nasal swab
- Stool: Stool sample
- Total: Sum of CSF, Nasal, and Stool samples

**References:**
- CDC. Increase in Acute Flaccid Myelitis — United States, 2018. MMWR Morb Mortal Wkly Rep 2018;67:1273–1275. DOI: http://dx.doi.org/10.15585/mmwr.mm6745e1

8/5/2019
Presentation in Japanese Patients

- 59 patients (1 with probable AFM); 8-12/2015
  - 7/20 positive with EV-D68 (3 resp, 3 stool, 1 CSF)
- Prodromal symptoms (97%)
  - Fever (88%), URI (75%), GI(19%)
- Limb paralysis (100%)
  - 1 (37%), 2 (39%), 3 (5%), 4 (19%)
  - Asymmetric (68%)
- Hyporeflexia (90%)
- Cranial nerve involvement (17%)
- Focal paresthesias (20%)

Presentation in Japanese Patients

- Imaging
  - All had longitudinal cord lesions
    - Median of 20 vertebral levels
  - Brainstem lesions in 42%
  - Enhancement
    - Parenchymal – 5%
    - Ventral nerve root – 15%
    - Cauda equina – 51%

Presentation in Japanese Patients

- EMG
  - Motor conduction abnormal in 82%
  - F-waves abnormal in 73%
- CSF
  - Pleocytosis in 85%
    - Greater if done earlier
  - Elevated protein in 46%
Cause of illness

- Direct infection of a virus on the motor neurons (nerves that make the muscles move)
- Indirect infection where a virus may lead to an inflammatory or immune response directed toward motor neurons
- Host genetic factors in which certain children may be more susceptible than others

https://www.cdc.gov/acute-flaccid-myelitis/afm-surveillance.html, accessed on 1/7/19

Cause

- When a pathogen is found in CSF it is likely the cause
- Most cases had no associated CSF pathogen
  – EV-A71, EV-D68, Cocksackie A-16 found in CSF in 4/512 cases
- Reasons for no CSF pathogen in most cases?
  – Pathogen is cleared by body
  – Pathogen is hiding in tissues
  – Pathogen triggers an immune response
- Unclear why few get AFM if many are infected with viruses

Known Viral Causes of Limb Paralysis

- Polio
- WNV
- EV-A71
- EV-D70
- Coxsackievirus A16 (CSF – 1 case)
- Japanese Encephalitis
- Hopkin’s Syndrome (AFP following asthma)
- EV-D68
Polio Virus

- Two types of Polio Virus
  - WT = wild type
    - 3 strains; only WT1 since 2012
  - cVDPV = circulating vaccine-derived poliovirus
- In 1988, polio was endemic in 125 countries, sickening and paralyzing 350,000 children
- Total of 32 reported cases of WTPV in Afghanistan and Pakistan during 2018
- Impacts primarily children <5 yo

Polio Virus

- No cases of polio in the USA since 1979
- Transmission is fecal-oral, contaminated food
- Clinical
  - Most people do not know they have it
  - Can present with fever, fatigue, headache, vomiting, stiffness, pain in limbs
  - 1-2% result in aseptic meningitis
  - 0.5% result in poliomyelitis
    - 5-10% of these die when respiratory muscles paralyzed
- None of the current AFM patients had stool positive for polio

Main Viral Findings in Recent AFM

- EV-D68
- EV-A71
  - Previously associated with brainstem encephalitis
Enterovirus/Rhinovirus Types

Ev-A71

- Isolated first in late 1960's
  - Clinically
    - Hand, foot and mouth disease
    - Aseptic meningitis
    - Encephalitis (Brainstem)
    - AFM
    - Transverse myelitis
    - GBS
  - Cyclical - Every 3 years
  - CSF yield is low, <30% for neurologic disease
  - Outcome
    - 56% with AFM has residual weakness/atrophy (12.5% in another study)
    - 80% had single limb involvement

Ev-D68

- Discovered in 1962
  - Pneumonia in California
- Non-polio enterovirus
- Similar to Rhinovirus 87.
- Respiratory transmission
- Not heat or acid stable
  - Not found in stool
- 26 cases found 1970-2005
- Clusters occurred in Europe 2008-2010
- Dramatic increase in 2014 (1153 cases)
- 6 Clades
  - B1 is the clade associated with AFM, evolved in 2010
EV-D68 Virus

Image source: Yue Liu and Michael G. Rossmann, Purdue University. The publication of this study was by Yue Liu, Ju Sheng, Andrei Fokine, Gang Meng, Woong-Hee Shin, Feng Long, Richard J. Kuhn, Daisuke Kihara, Michael G. Rossmann (all at Purdue University)

Association of AFM, EV-D68

• Bradford Criteria
  – Strength
  – Specificity
  – Consistency
  – Specificity
  – Temporality
  – Biological Gradient
  – Plausibility
  – Coherence
  – Experiment
• 6 are fully met, 2 (specificity and strength) are partially met, and 1 (biological gradient) is minimally met

Dyda A. Euro Surveill. 2018 Jan;23(3)
Cause

- Strong association with EV-D68 temporally, in respiratory secretions, but not in CSF (affected tissue)

Treatment

- No indication that any specific targeted therapy/intervention should be preferred or avoided in treatment of AFM
- Should obtain neurology and/or infectious disease consult
- Respiratory monitoring
  - Negative inspiratory force
  - Forced vital capacity

Types of Treatment Used

  - IVIG – 74%
  - Plasmapheresis – 17%
  - IV Steroids – 58%
  - Antivirals – 5%
- Japan (2015)
  - IVIG – 19%
  - IV steroids – 15%
  - Steroids + IVIG – 59%
  - Plasmapheresis – 5%
Treatment

- Corticosteroids – may help with spinal cord edema, but is harmful in mouse model of EV-D68; can also result in immunosuppression.
- IVIG – no evidence for harm or benefit
  - Beneficial in mouse model (Viral load for EV-D68 is low)
- Plasmapheresis – no evidence of benefit; risk associated with procedure
- Fluoxetine – no evidence for efficacy
- Antiviral medications – no evidence for efficacy
- Interferon – no evidence for efficacy
- Immunosuppressant (other) - no evidence for efficacy

https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinical-management.html

Treatment

- Treatment decisions should be made in conjunction with neurology and infectious diseases 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 other immunosuppressive agents in the management of AFM
- 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 are currently no data to indicate benefit

Nerve transfers

- A stepwise surgical algorithm using nerve transfers for the treatment of upper extremity acute flaccid myelitis
  Erin L Weber, et.al.
Outcome Study #1

• 12 Children from Colorado 2014 outbreak
  – 8 completed year long study
    • 2 with full recovery
    • 6 with persistent deficit
      – Proximal muscles with atrophy
  – 2 that didn’t complete study reported full recovery
  – Cranial nerve dysfunction resolved in 2/5
    • Diplopia, Facial weakness, bulbar weakness
    • Improved in all

Outcomes of Colorado Cases at 1 year

• 12 Cases
• KM plot
• Muscle atrophy

Outcome Study #1

• Additional findings
  – Pain (2/8)
  – Depressive symptoms (3/8)
  – MRI significant improvement/normalization (6/8)
    • No enhancement
  – Repeat EMG/NCS showing ongoing denervation/chronic reinnervation (3/4)
    • Better correlated with outcome than MRI
• Despite improvement, AFM had substantial long-term functional effects on affected kids
Outcome Study #2

• 16 patients from Johns Hopkins
  – MRI showed improvement in spine
    • Worse in cervical, lumbar regions
  – No patient had complete functional recovery
    • 4 month f/u
    • Distal improved more than proximal
    • 15/16 had flaccid muscle tone
    • 16/16 had decreased/absent reflexes
  • 4/16 required mechanical ventilation
  • 0/16 with sensory changes


Outcome Study #3

• 14 children from CHOP
  – 5 from 2014, 9 from 2016
  – Evaluated in 2017
  – Of the 2014 group, 4/5 had significant improvement
  – Of the 2016 group, all have significant weakness


Outcome Study #4

• 59 Cases from Japan (2015)
  – Complete motor functional recovery – 12%
    • Better for CN, paresthesias, bladder
  – 68% with muscle atrophy
  – Good outcome with normal F-wave
  – Poorer outcome with IVIG, steroid Rx

Outcome Study #5

- 28 patients at Kaiser Permanente
- Recovery not predicted by initial presentation
- At 12 months, 2 patients required a trach, 4 patients had a G-tube
- On death at less than 18 months from complications

<table>
<thead>
<tr>
<th>Improvement</th>
<th>Discharge</th>
<th>Within 6 months</th>
<th>Within 12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Partial</td>
<td>24</td>
<td>19</td>
<td>16</td>
</tr>
<tr>
<td>Full Recovery</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Additional Outcomes

- 2/5 ventilator dependent at 18 months
- Of 120 cases identified by CDC in 2014
  - 56 with f/u (median 4 months)
  - Only 3 with complete recovery
    - 14% fully dependent
    - 68% with some impairment
    - 18% fully functional
- Of 21 in Canadian Cohort
  - 2 fully recovered
- CDC announced it will follow outcomes now

Prevention

- Vaccination against polio virus
- Avoid WNV with mosquito repellant
- Avoid enteroviruses by avoiding contact with sick people, good handwashing.
- New vaccines?
  - China has developed vaccine for EV-A71
- Anti-virals?
  - Enviroxime, Pirodivir, Pleconaril, Ribavirin, Rupinintravir and guanidine
Future Directions

- Understand underlying mechanism of AFM
  - Viral vs. postviral
- Determining host risk factors
- Evaluate treatments (Antivirals, Immunosuppressants)
- Develop vaccines
- Determine long-term outcome

CDC Form for AFM

Public Health England Form
Impact of Flu

Reference Images

References

- Council of State and Territorial Epidemiologists – 17-ID-01
References


