



**“Polio-like syndrome”
A long forgotten nightmare**

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Objectives

- **Define acute flaccid myelitis (AFM).**
- **Spotlight on recent outbreaks.**
- **Identify the causative pathogens.**
- **Identify the collaborative efforts needed to understand and prevent the disease.**
- **Prevention.**

We all remember polio!!



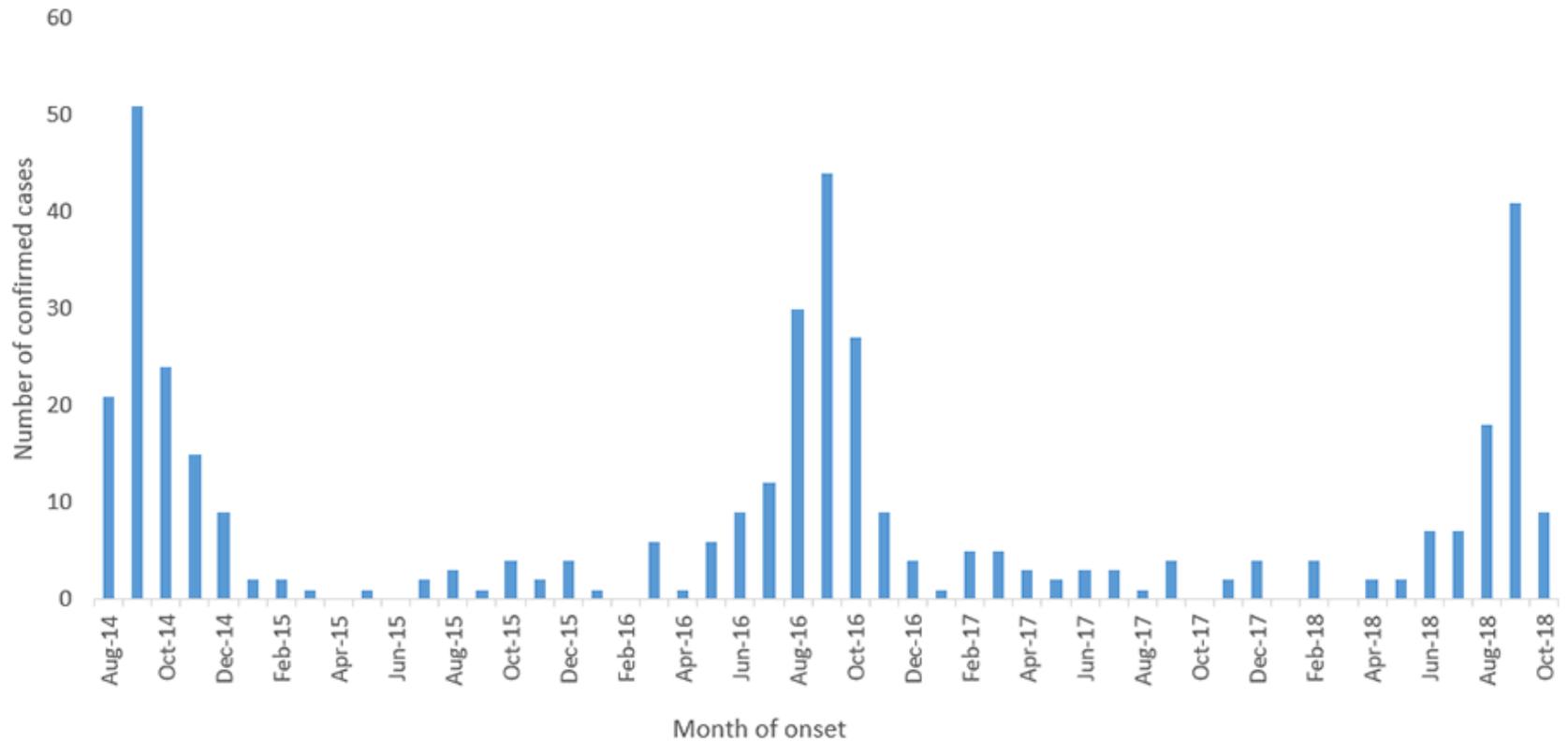
Background

- **In 2016, the Region of the Americas was celebrating in USA 25 years with no cases of wild poliovirus.**
- **At the same time, CDC was investigating the increase in AFM in 2016, as a mysterious disease resembling polio has been on the rise since 2014.**





Number of confirmed U.S. AFM cases reported to CDC by month of onset, August 2014 - October 2018^{^†}





Definition

- Acute flaccid myelitis (AFM) is a condition that affects the nervous system, specifically the spinal cord, which can result from a variety of causes including viral infections.
- AFM is characterized by a sudden weakness in one or more arms or legs, along with loss of muscle tone and decreased or absent reflexes



Symptoms

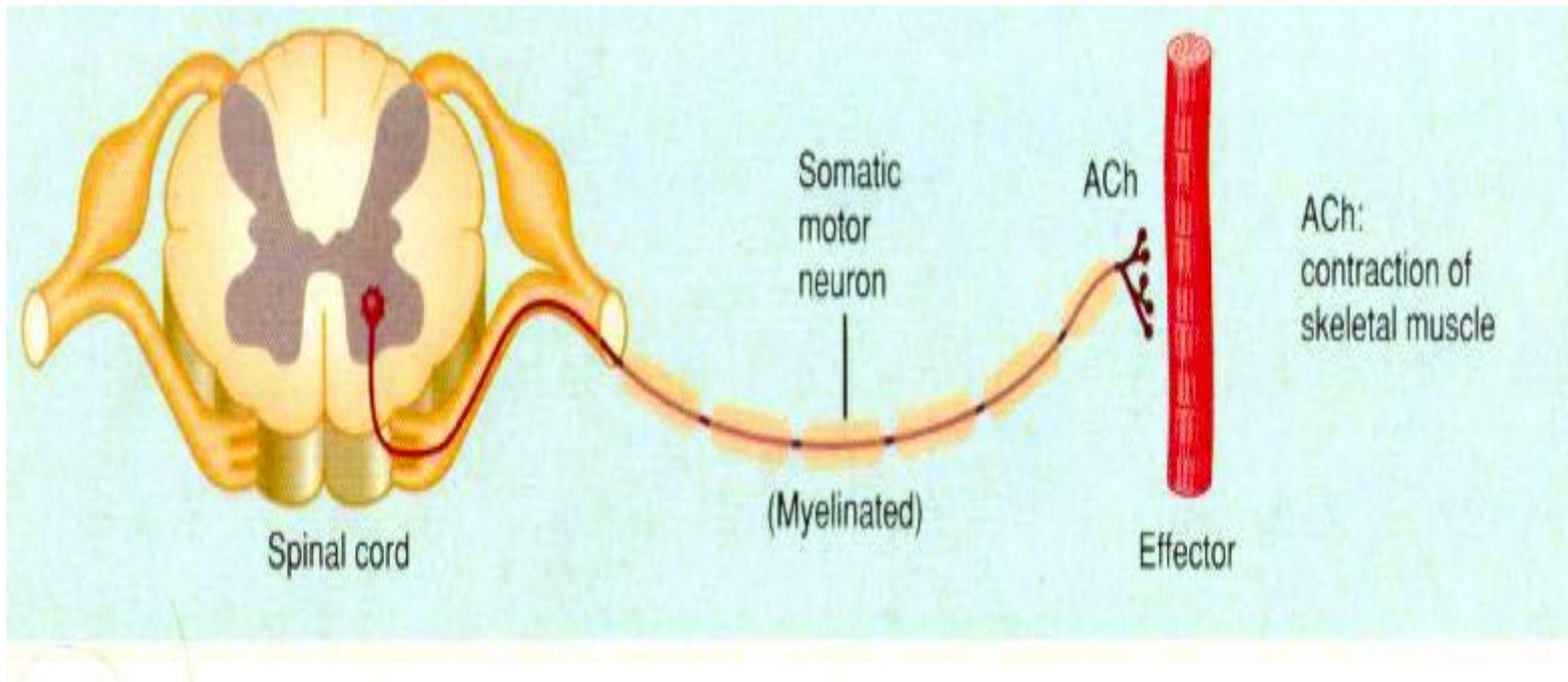


- Most patients will have sudden onset of limb weakness and loss of muscle tone and reflexes.
- Some patients, will also experience:
- facial droop/weakness, difficulty moving the eyes, drooping eyelids, or difficulty with swallowing or slurred speech due to cranial nerve affection .

- Some patients with AFM may be unable to pass urine.
- The most severe symptom of AFM is **respiratory failure.**
- Most of the affected patients are **children .**



Areas of the Spinal Cord Affected by AFP



The lesion may be anywhere along the neuroaxis from lower motor neuron onward.



Causes of AFM:

❖ Viral infections.

❖ Environmental toxins.

❖ Genetic disorders

❖ Guillain-Barre syndrome.

- Oftentimes, however, despite extensive laboratory testing, a cause for AFM is **unable to be identified.**



Viral AFM

- AFM is most commonly associated with **poliovirus**, but may be caused by numerous other viral pathogens:
 - **Non-polio enteroviruses.**
 - Flaviviruses (West Nile virus, Japanese encephalitis virus)
 - Herpesviruses.
 - Adenoviruses .

- Respiratory illnesses and fever from viral infections such as enteroviruses are common, especially in children, and most people recover.
- A small number of patients develop AFM, while most others recover. Possible explanations:
 - A **direct infection** of a virus on the motor neurons (nerves that make the muscles move)
 - An **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



- Since the ongoing successes at eliminating wild-type polio from most of the world, this syndrome has become exceedingly rare.
- **GBS** is now the leading cause of AFP worldwide.

- Because 'poliomyelitis' connotes infection with poliovirus and none of the specimens from recent cases with this 'polio-like' illness tested positive for poliovirus, the term 'acute flaccid myelitis', or AFM, was used to describe the cases that occurred in the summer / fall of 2014.



- During the summer of 2014, the Centers for Disease Control and Prevention (CDC) reported an unusual increase in the frequency of acute flaccid myelitis among children in the United States.
- This outbreak occurred coincidentally with an outbreak of respiratory disease caused by **enterovirus D68 (EV-D68)**.

Picornaviridae

www.emmasaying.com



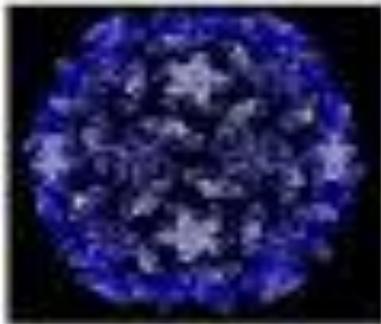


Picornaviruses

Pico rna viruses

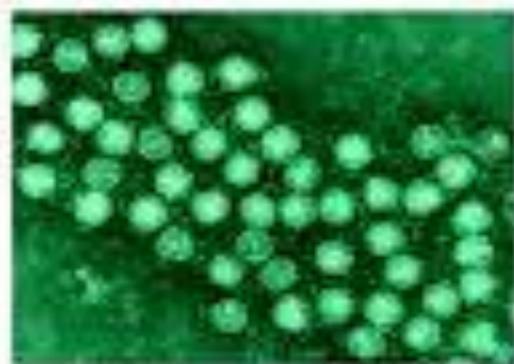
Pico = small

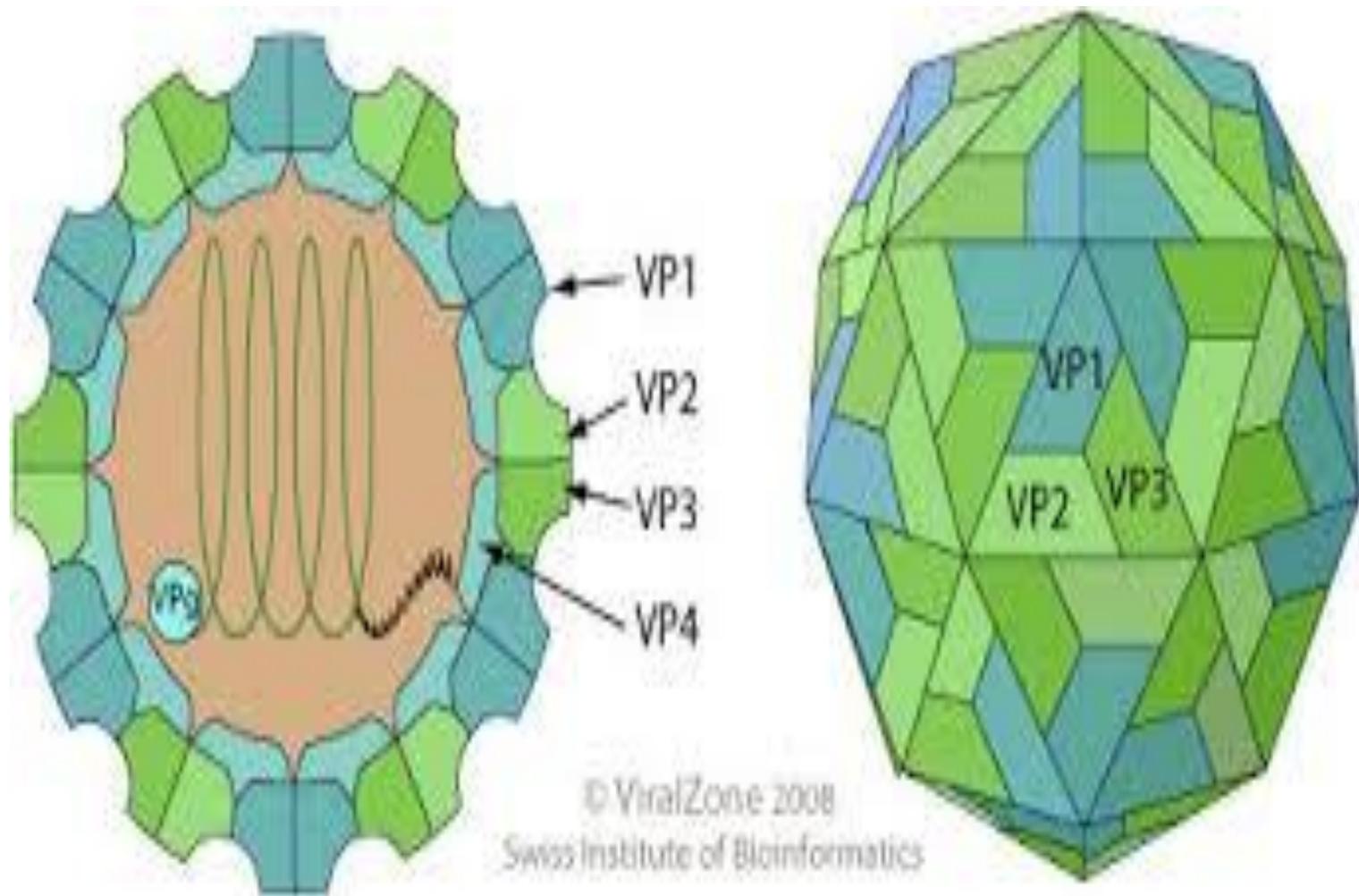
rna = RNA



Structure of virion

- Ss +RNA.
- Virion is icosahedral 22-30nm in diameter.
- Capsid has 60 copies of 4 proteins:
 - VP1, VP2, and VP3 are exposed on the virion surface,
 - VP4 lies buried in close association with the RNA core.
- Immunogenic sites are located on the external parts of the capsid.







Classification

- The family Picornaviridae includes:
 - **Enteroviruses:**
 - poliovirus,
 - Coxsackieviruses,
 - echoviruses,
 - Other enteroviruses (68-71)
 - **Rhinoviruses**
 - **Hepatitis A virus**



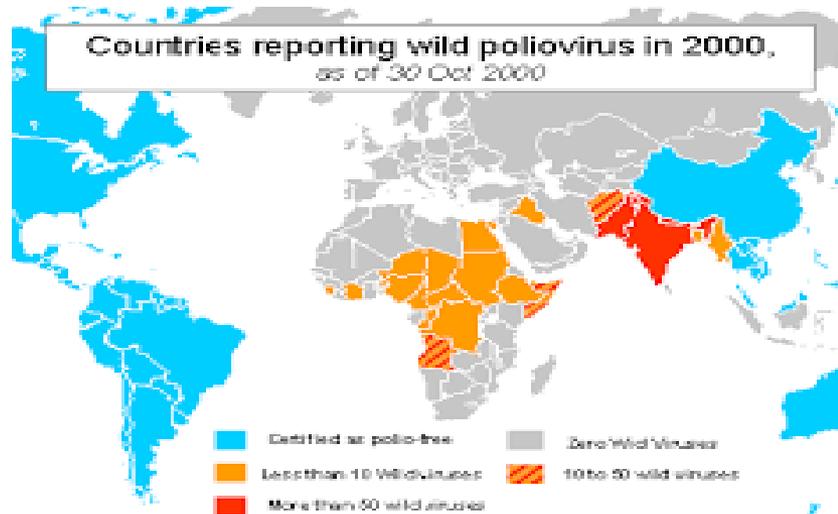
Poliovirus

- Poliomyelitis has appeared in epidemic form, become endemic on a global scale, and been reduced to near elimination.



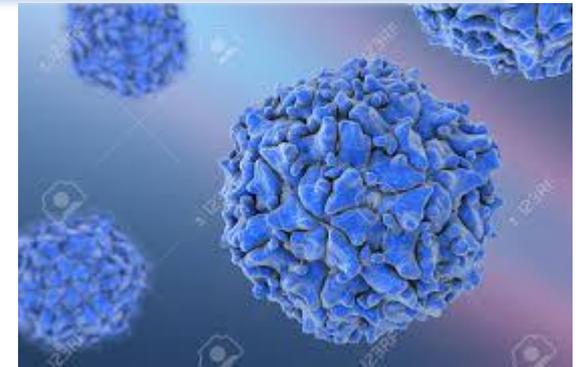
History of polio...

The disease of poliomyelitis has a long history. The first example may even have been more than 3000 years ago. An Egyptian stele dating from the 18th Egyptian dynasty (1580 - 1350 BCE) shows a priest with a deformity of his leg characteristic of the flaccid paralysis typical of poliomyelitis.





- Poliovirus (PV), a human enterovirus (has three known serotypes: **PV1, PV2, and PV3** .
- All three PV serotypes can cause poliomyelitis.
- The three-dimensional atomic structures of PV1, PV2, and PV3 have very similar structural features among themselves, which are also similar to those of other human enteroviruses and rhinoviruses.
- All three serotypes of PV recognize a common cellular receptor, **CD155** for cell attachment and entry





The last case of poliomyelitis was recorded in Egypt in 2004 in Assiut.



- <http://www.who.int/biologicals/areas/vaccines/poliomyelitis/en/>



Enteroviruses

- Enteroviruses have several subgroups:
 - 3 serotypes of **polioviruses**,
 - 23 serotypes of group A **coxsackieviruses**,
 - 6 serotypes of group B coxsackieviruses,
 - and at least 31 serotypes of **echoviruses**
 - Some enteroviruses are not classified further but rather assigned a number, 68 to 71..



- Enteroviruses grow at a wide pH range (ie, 3-10). After initial replication in the oropharynx, enteroviruses survive the acidic environment of the stomach. The small intestine is the major invasion site of enteroviruses, which replicate best at 37°C.
- Rhinoviruses replicate at a pH of 6-8. After initial replication in the nasal passages, the acidic environment of the stomach destroys rhinoviruses. Rhinoviruses optimally replicate at 33°C and primarily infect the nasal mucosa.



- Diseases due to EVs range from febrile illnesses to myopericarditis, paralysis or encephalitis, with a significant number of complications and deaths. EVs are notably the most frequent cause of **viral meningitis**.
- However, some types of EVs are only found in the respiratory tract and cause RV-like symptoms, especially EVs from species C and D and are consequently named **respiratory EVs**.



Recent Re-Emergence of EV-D68 and Other Respiratory EVs

- **EV-D68 :**
- is a member of the small EV-D species and was first isolated in 1962 in California, USA, in respiratory samples of four children with respiratory disease.
- Due to its biological properties, such as the typical acid lability of RV and an optimal growth temperature of 33 C, EV-D68 is of particular interest because it shares characteristics of both RV and EV.



- Rarely observed until the late 2000s, a few clusters of EV-D68 cases were progressively reported in different parts of the world during the last decade and associated with mild to severe respiratory illness .
- During autumn 2014, the USA experienced the largest outbreak of EV-D68 especially in the pediatric population. A total of 1153 individuals in 49 states tested positive for this virus, mostly children, many with a previous history of wheezing or asthma.

Changing epidemiology





- This rapid increase in reported cases over the last few years was first believed to be caused by the improvement of detection techniques and to the previous misidentification of EV-D68 as a RV leading to an underestimated prevalence.
- However, retrospective tests confirmed this real increase in prevalence . Phylogenetic analysis of recently detected EV-D68 strains revealed an increased diversity in VP1 sequences.



- These strains cluster in three different genetic lineages, which are clearly distinguishable from the prototype strains.
- **Some amino acids changes (mostly substitutions but also one deletion) in the capsid encoding genes, predominantly in VP1,** define these different lineages.



- **These emergent strains have highly different antigenic properties, which could have impacted greatly on the transmission dynamics of the virus and may explain the epidemiological change.**

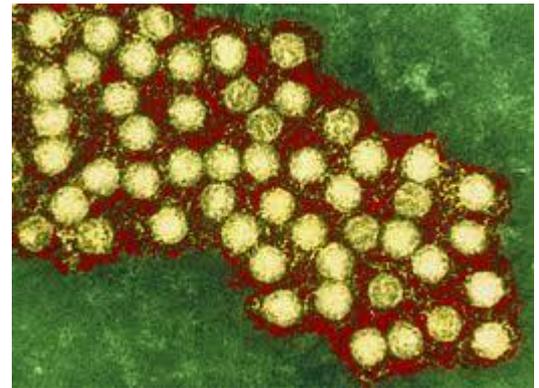


Other enteroviruses:

- **Enterovirus A-71**
- **EV-D70** (a close relative of EV-D68).
- **Coxsackievirus A24** variant (CVA24v, member of EV-C) can also cause AFM and have a pandemic potential.
- **Enterovirus C105**

Pathogen recognition

- ❖ Enterovirus (including poliovirus), EV-D68 PCR.
- ❖ Adenovirus PCR.
- ❖ Herpesviruses PCRs.
- ❖ Arbovirus serology.
- ❖ ????????





Laboratory Diagnosis



Specimen Collection

Collect specimens **as early as possible** in the course of illness, preferably on the day of onset of limb weakness.





EACH of the following specimens is requested:

- **CSF**
- **Upper respiratory tract specimen** Nasopharyngeal swab >> Nasal swab >> Nasal wash/aspirate
- **Serum:** 2-3 cc collected
- Acute: Collect as soon as possible.
- Convalescent: Collected 10-14 days after first serum
- Two **stools** collected 24 hours apart.



Laboratory workup



- PCR assays for enteroviruses, including poliovirus, and EV-D68.
- PCR assays for adenovirus, herpesviruses.
- arbovirus serology

Treatment

- There is no specific treatment for AFM
- A neurologist may recommend certain interventions on a case-by-case basis.
e.g. physical or occupational therapy to help with arm or leg weakness caused by AFM.

Infection Prevention and Control

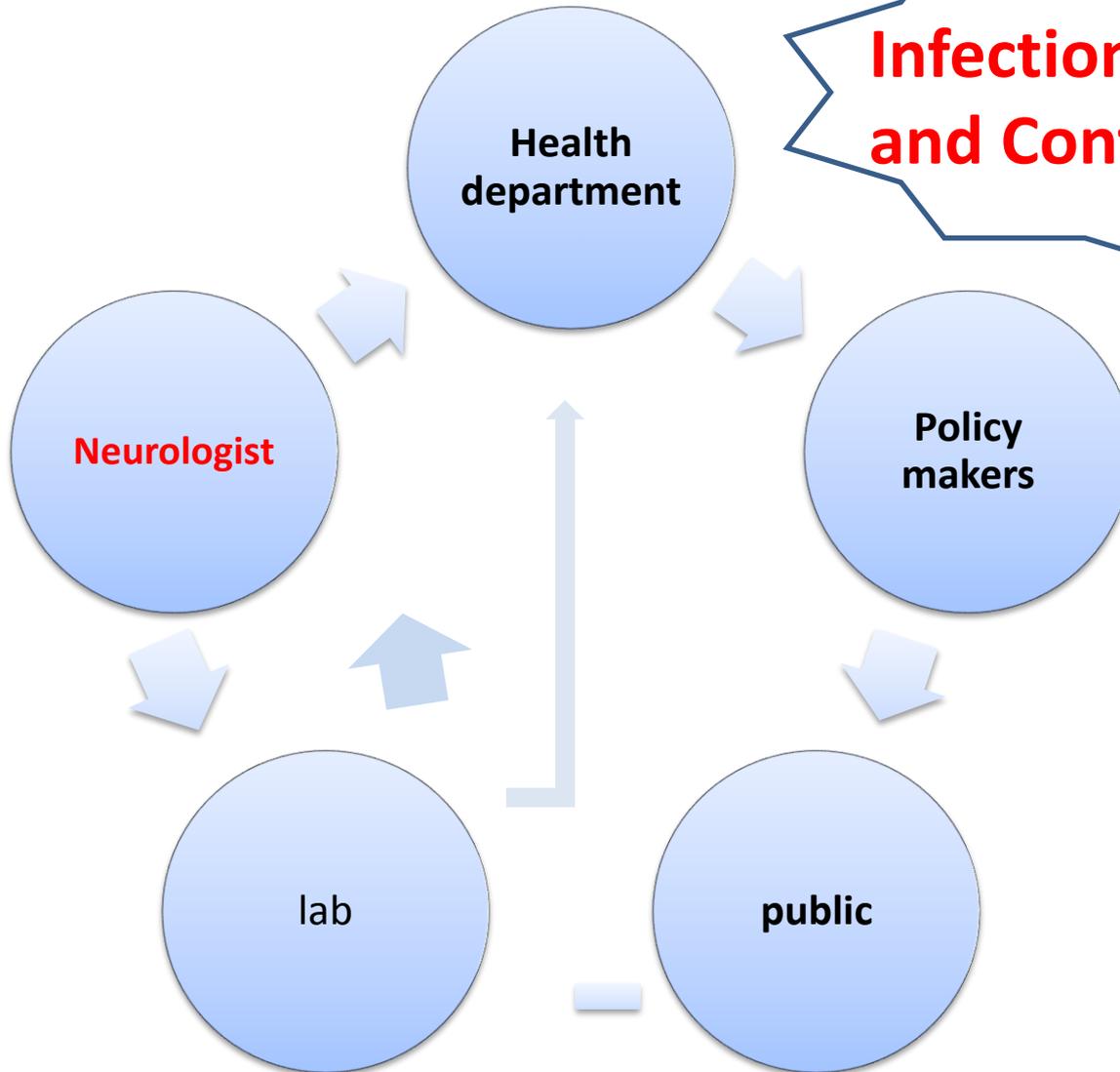


- **AFM is a serious disease that requires the integrated and collaborative efforts of all concerned parties.**
- **The prevention and control include an active surveillance program, in addition to hand hygiene, vaccination and isolation of cases.**

Surveillance



Infection Prevention and Control



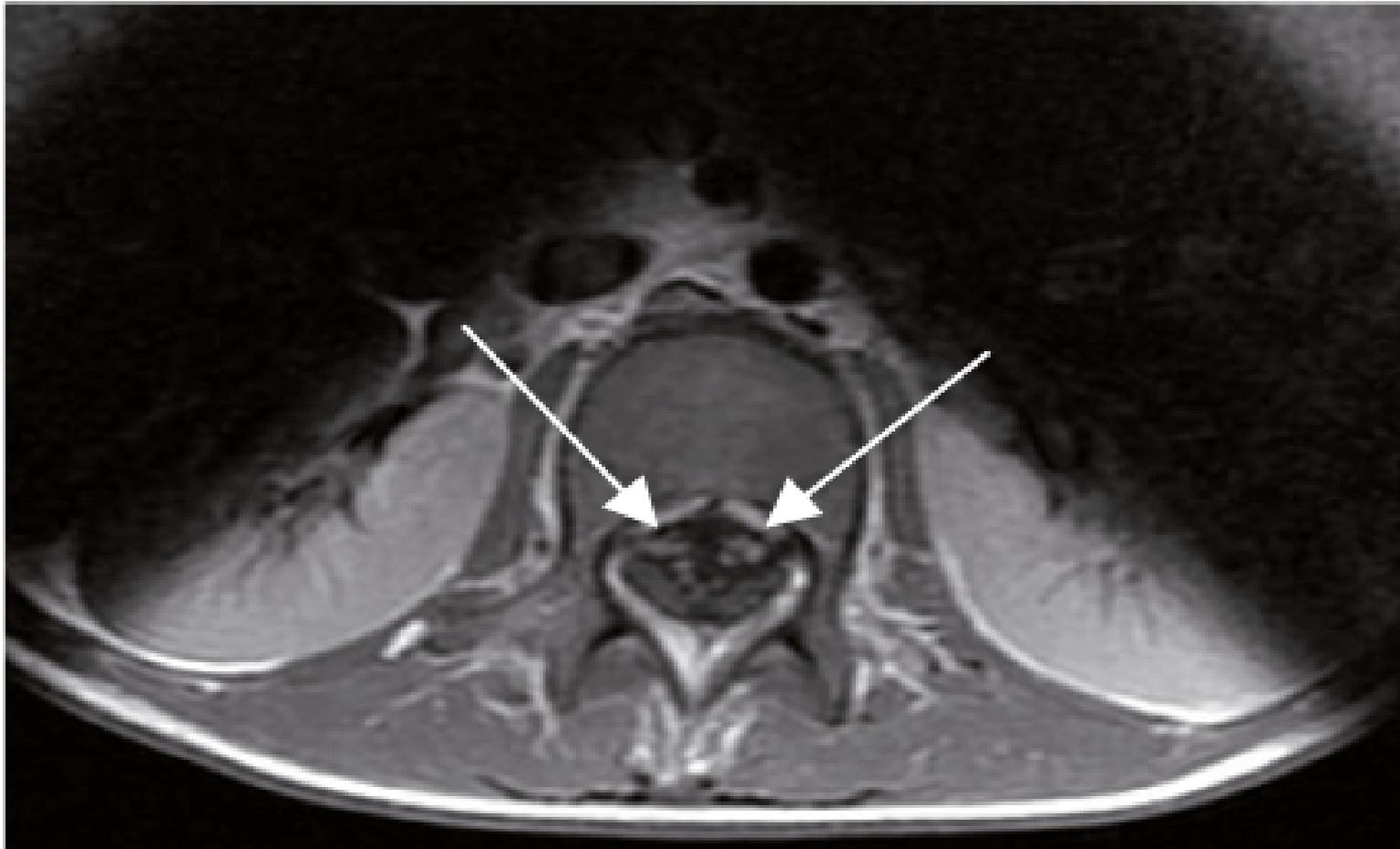


CASE DEFINITION: (CSTE*)

- **Clinical Criteria** An illness with onset of acute flaccid limb weakness
- **Laboratory Criteria**
- **Confirmatory Laboratory Evidence:** MRI showing spinal cord lesion largely restricted to gray matter and spanning one or more vertebral segments
 - **Supportive Laboratory Evidence:** CSF with pleocytosis (white blood cell count >5 cells/mm³)

*Council of state and territorial epidemiologists

Spinal magnetic resonance image, acute flaccid paralysis case following enterovirus D68 infection, France, 2014





Case Classification:

Case classification

Confirmed

- Clinically compatible case AND Confirmatory laboratory evidence

Probable

Clinically compatible case AND Supportive laboratory evidence

Sources of data

- Clinician reporting
- Laboratory reporting
- Death certificates
- Hospital discharge, neurology or infectious disease consult notes, MRI reports and images, or outpatient records
- Extracts from electronic medical records
- Telephone survey
- School-based survey

- **Isolation of patients ???????.**
- **Vaccination for poliovirus.**
- **Hand hygiene.**
- **Respiratory hygiene and cough etiquette**
- **Prevention of mosquitoes bites (mosquito repellants., staying indoors at dusk and dawn etc..)**





THANK YOU
FOR YOUR
TIME