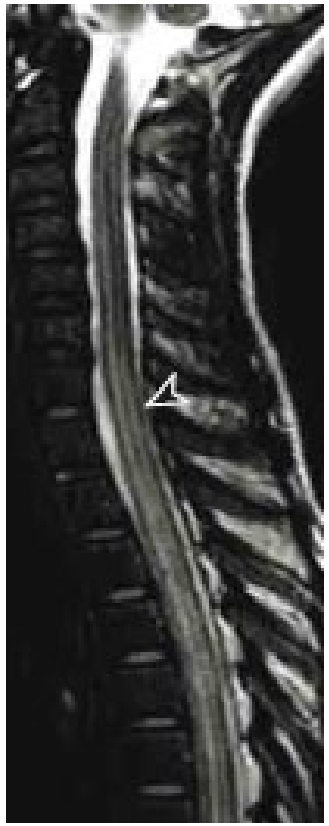
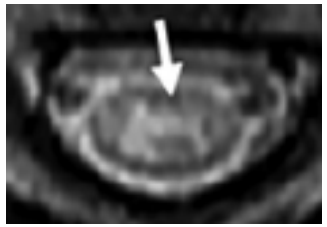
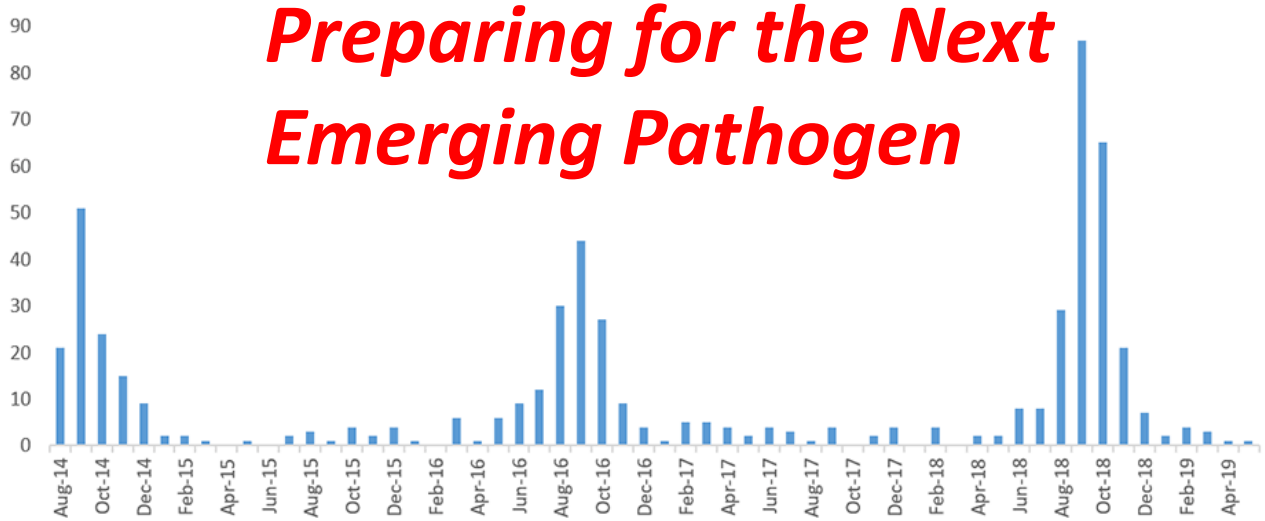
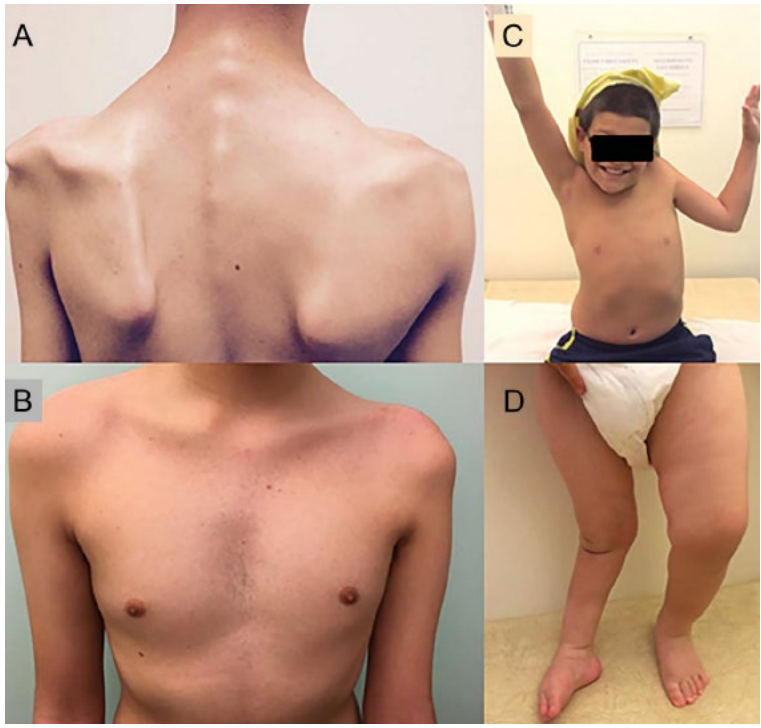
Enterovirus Acute Flaccid Myelitis





Preparing for the Next Emerging Pathogen





Kevin Messacar, MD PhD

Associate Professor of Pediatric Infectious Diseases
University of Colorado/ Children's Hospital Colorado
(kevin.messacar@childrenscolorado.org, @kmess44)

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Disclosures

- No relevant financial disclosures or conflicts of interest
  - Supported by NIAID K23AI28069

- I will discuss off-label use of medications

Please refrain from taking photos of any slides with the icon in the corner.

Fall 2014:

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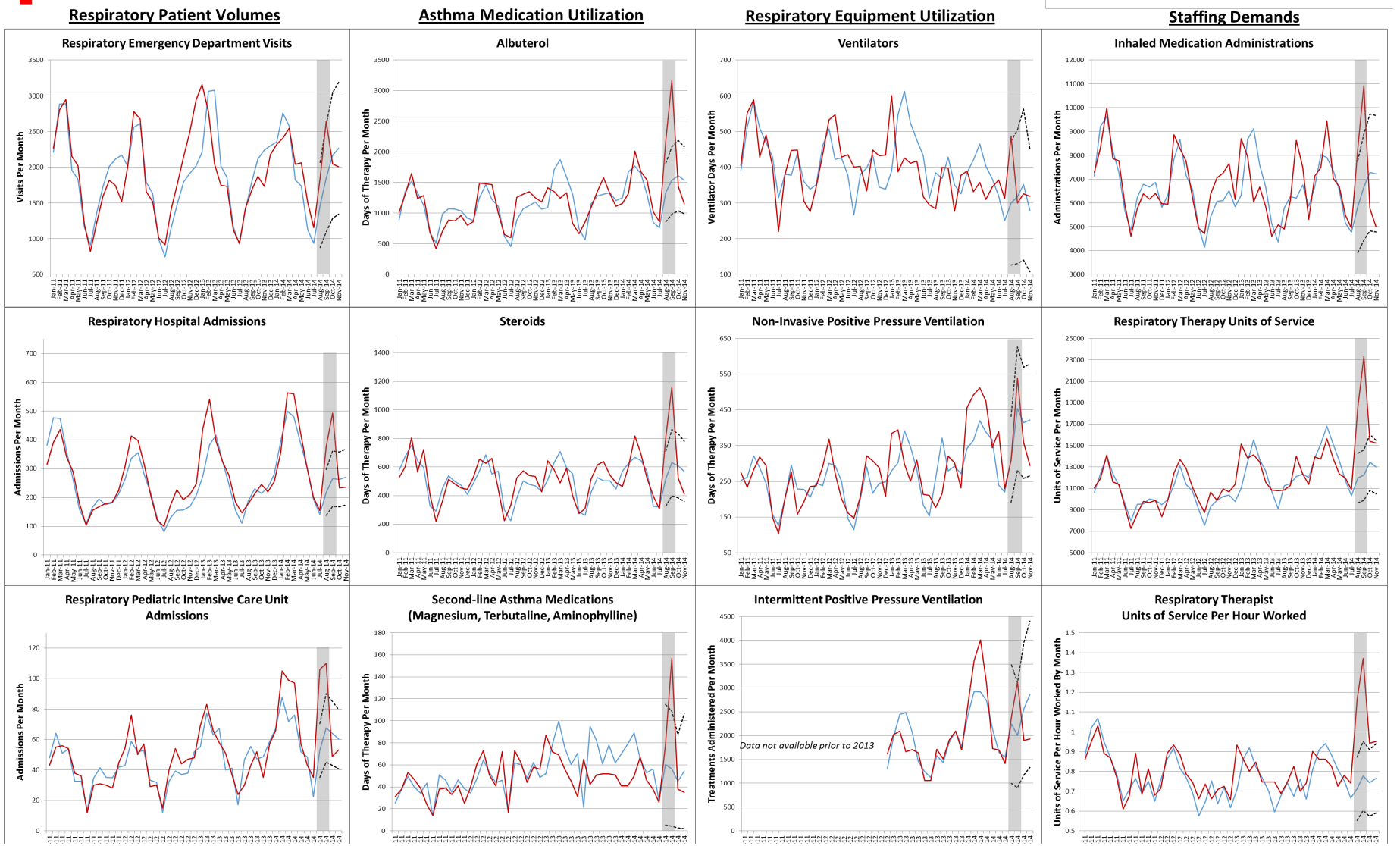
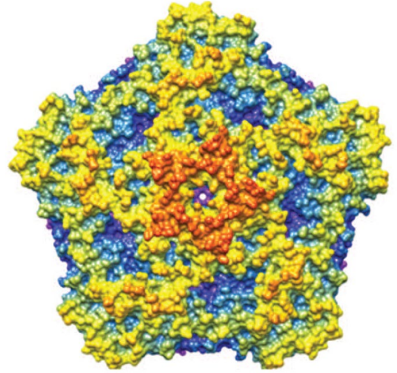
Fall 2014 Children's Hospital CO:
An Unexpected Strain

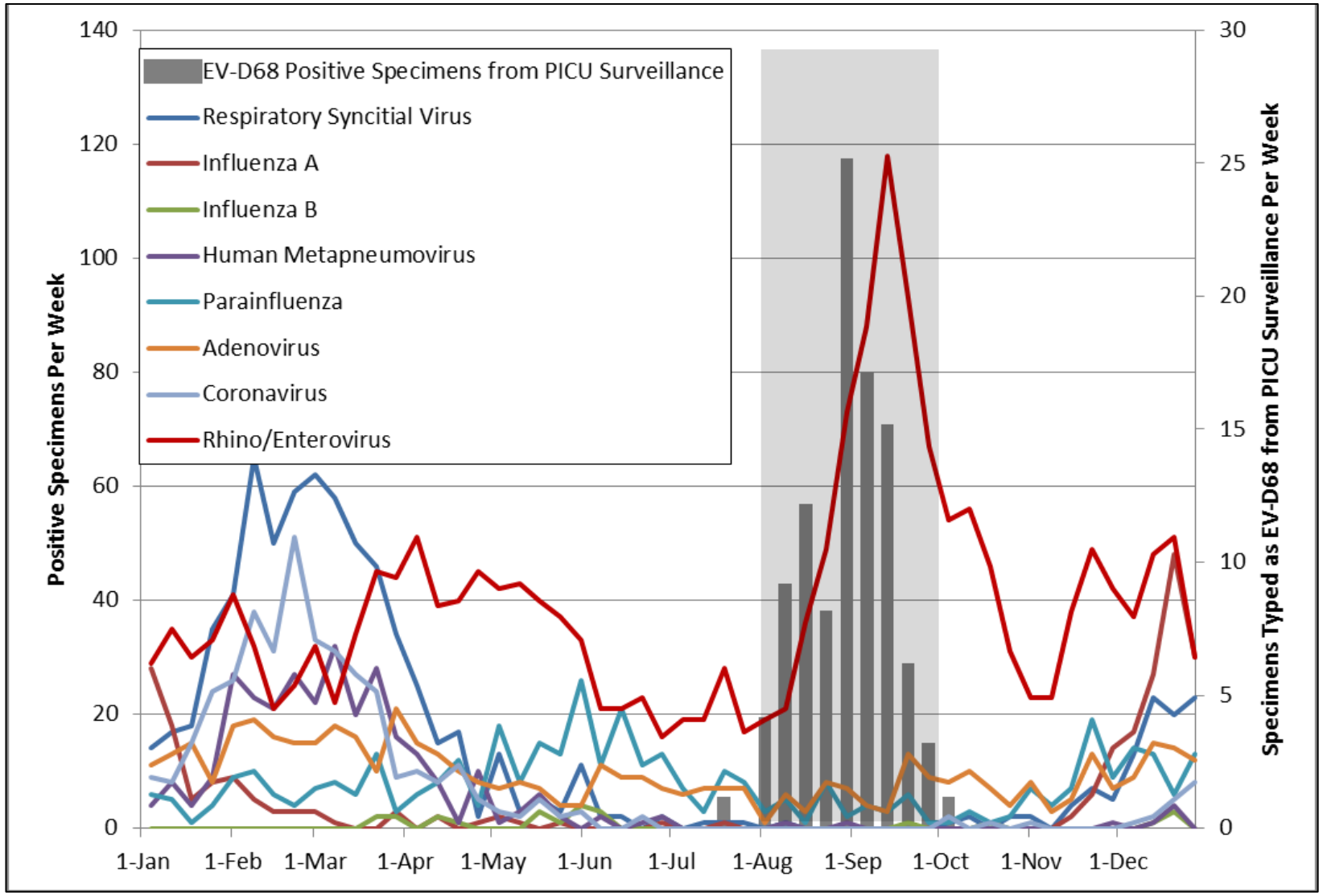
- **1185 Excess Respiratory ED Visits**
- **387 Excess Respiratory Admissions**
- **96 Excess Respiratory PICU Admissions**



Messacar et al. (2017) An Unexpected Strain: Resource Burden of the 2014 Enterovirus D68 Respiratory Outbreak at Children's Hospital Colorado. *JAMA Pediatrics*

The Unexpected Guest





Adapted from Rao S, Messacar K, Torok MR, et al. (2016) Enterovirus D68 in Critically Ill Children *Pediatr Crit Care Med.*

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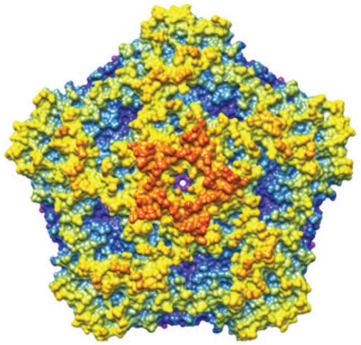

Enterovirus D68

- Discovered 1962 in respiratory specimens from children with pneumonia
- Non-polio EV: biological and clinical properties similar to rhinoviruses
- Can be acid labile
  - Unlike other EVs, broken down in GI tract and rarely detected in stool
- Optimal growth at 33°C
  - Transmitted by respiratory droplet, causes primarily respiratory disease

Messacar, K., et al. (2016). "The Emergence of Enterovirus-D68." *Microbiol Spectr* **4**(3).

2014

Aliabadi N, Messacar K, Pastula DM, et al. Enterovir

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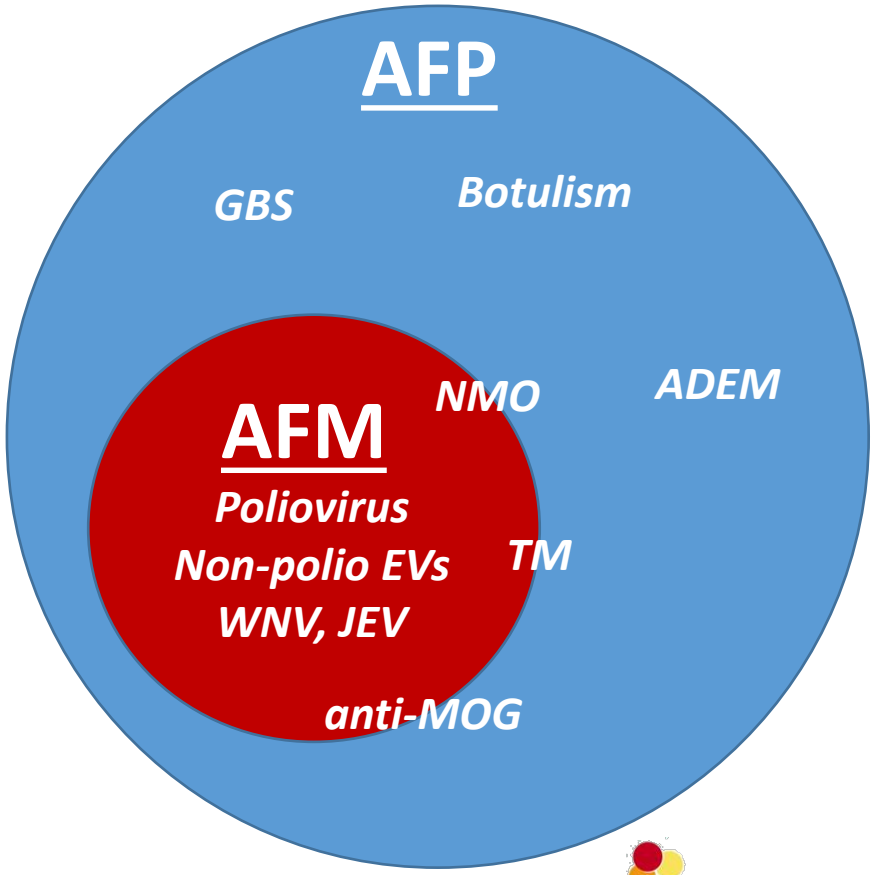
Case Definition:
Acute Flaccid Myelitis

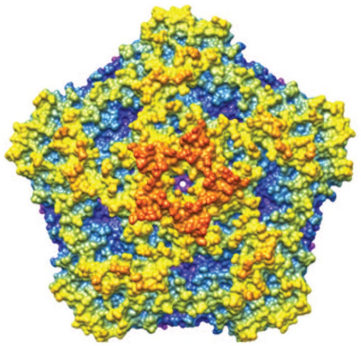
- **Clinical criteria**: Acute onset flaccid limb weakness (AFP)

+ Imaging criteria: MRI with spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments ("confirmed")



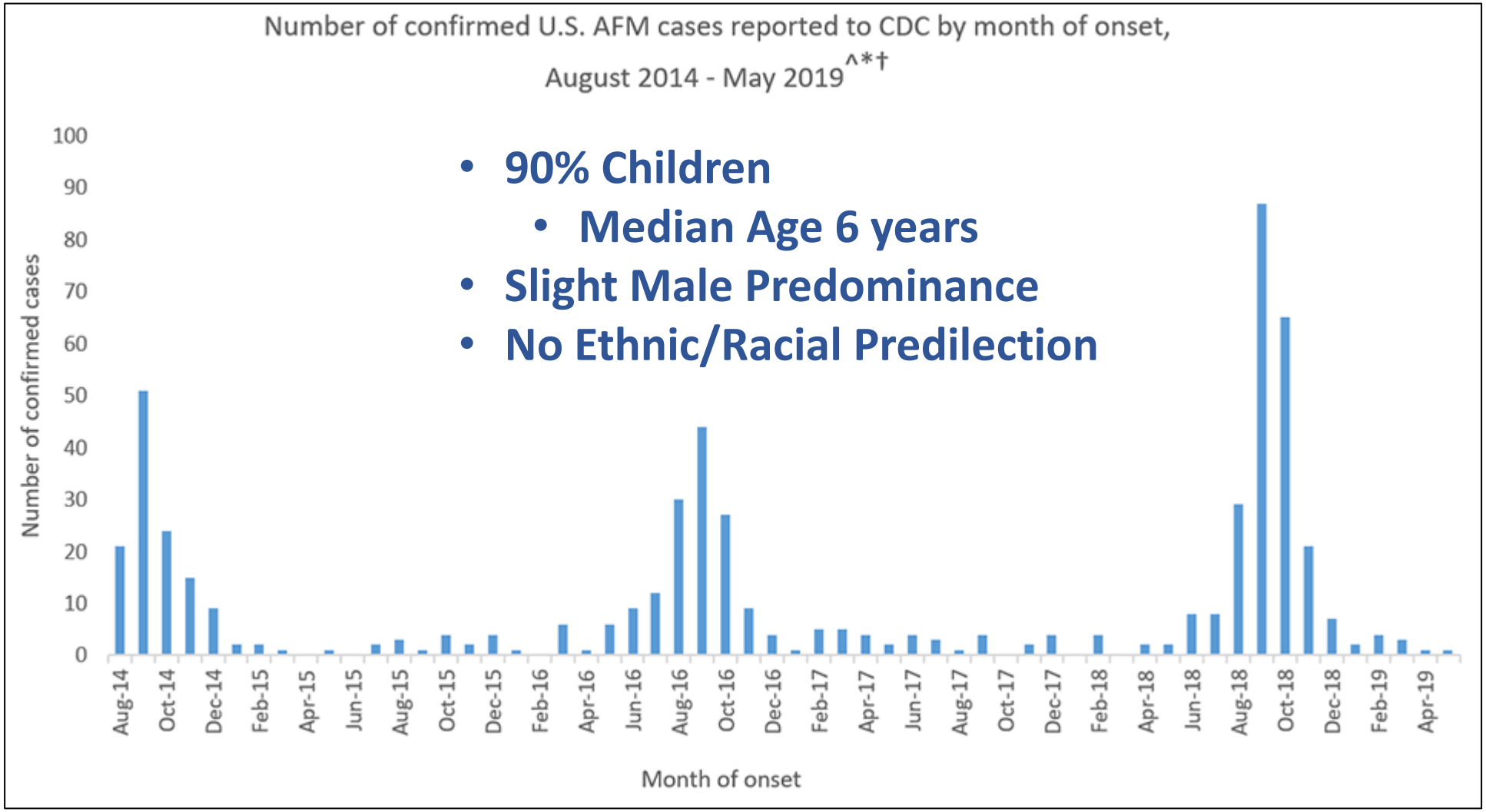
Council of State and Territorial Epidemiologists. Standardized Case Definition for Acute Flaccid Myelitis. 2015; http://c.ymcdn.com/sites/www.cste.org/resource/resmgr/2015PS/2015PSFinal/15-ID-01.pdf. Accessed October 30, 2015.

Outline

- Epidemiology
- Natural History
- Diagnosis
- Treatment
- Rehabilitation
- Outcomes
- 
  Research Developments

…Future Challenges

US AFM Epidemiology: 2014 - 2019



- **2014: 120 cases**
  - 34 states
- 2015: 22 cases
  - 17 states
- **2016: 153 cases**
  - 39 states
- 2017: 38 cases
  - 17 states
- **2018: 238 cases**
  - 42 states
- 2019: 47 cases
  - 18 states

https://www.cdc.gov/acute-flaccid-myelitis/afm-cases.html Accessed 7/7/21

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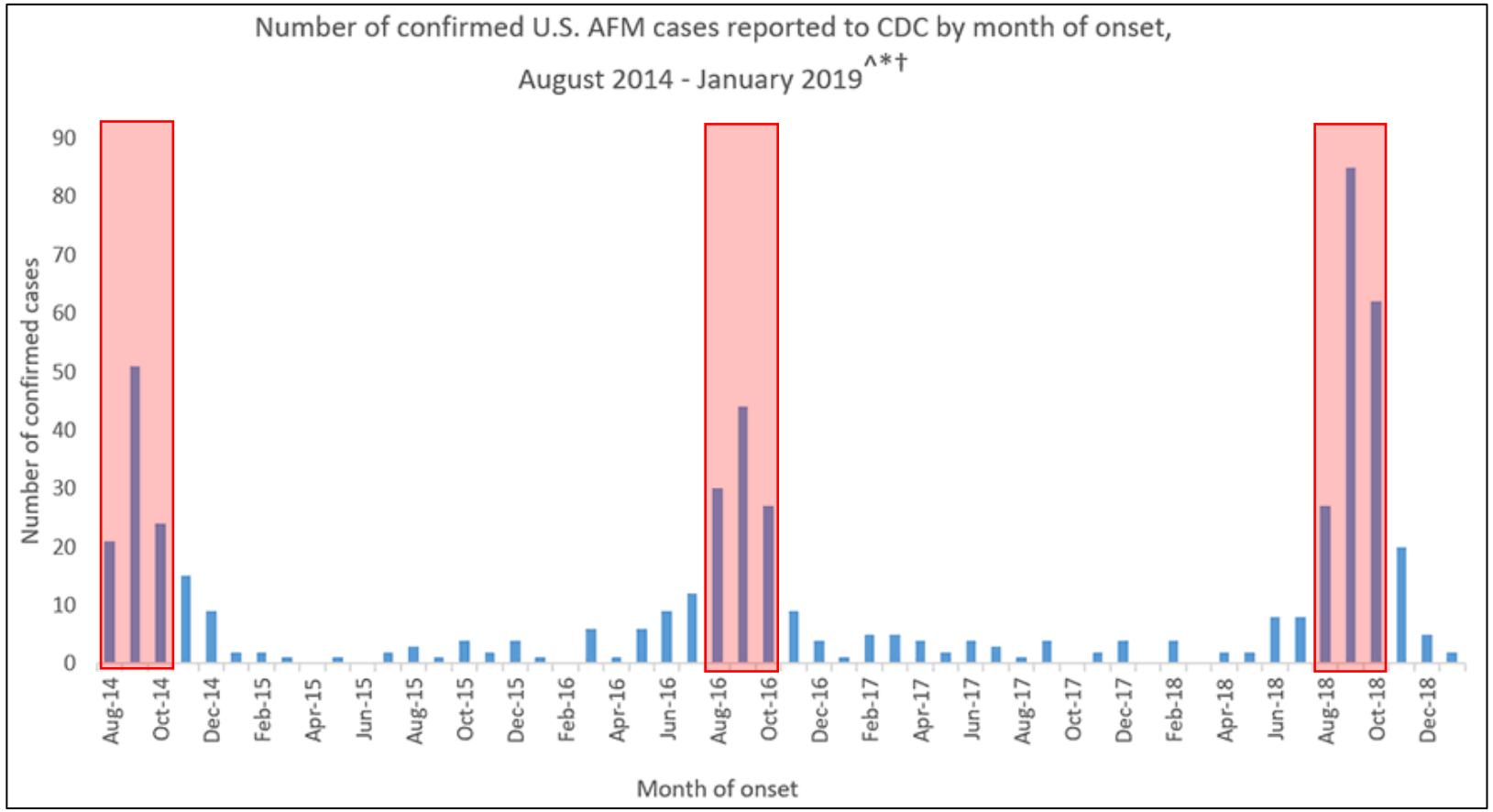
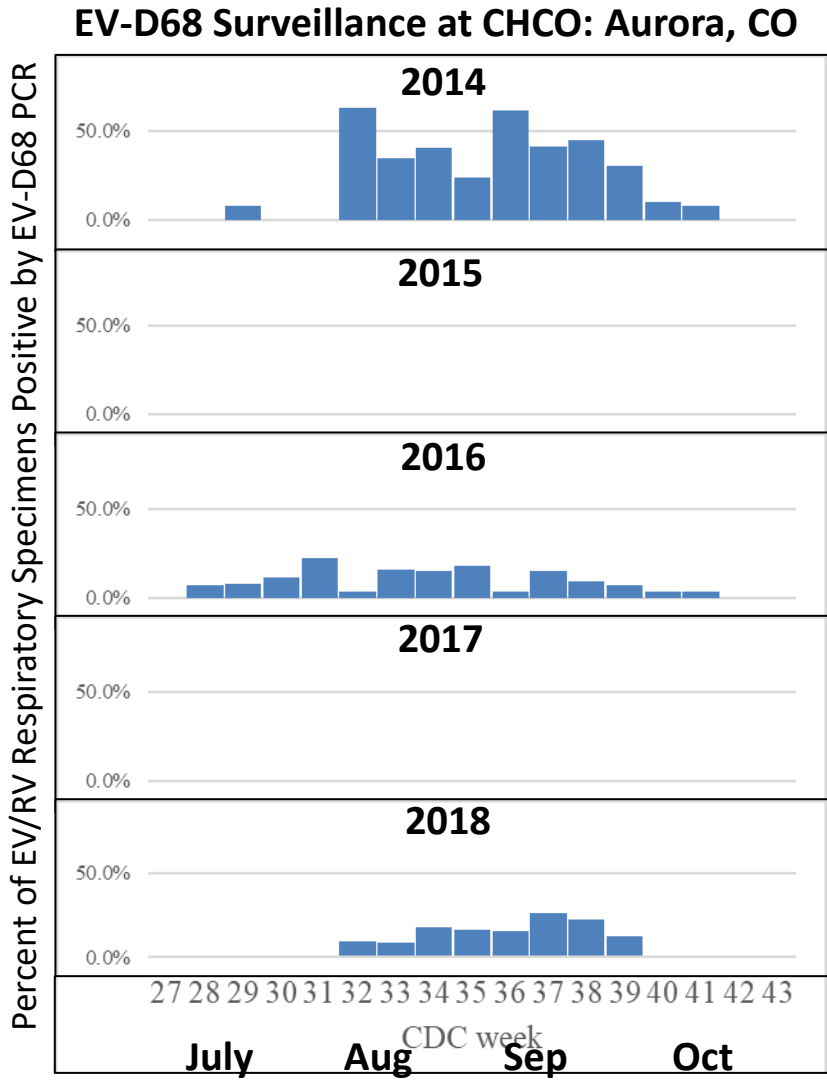
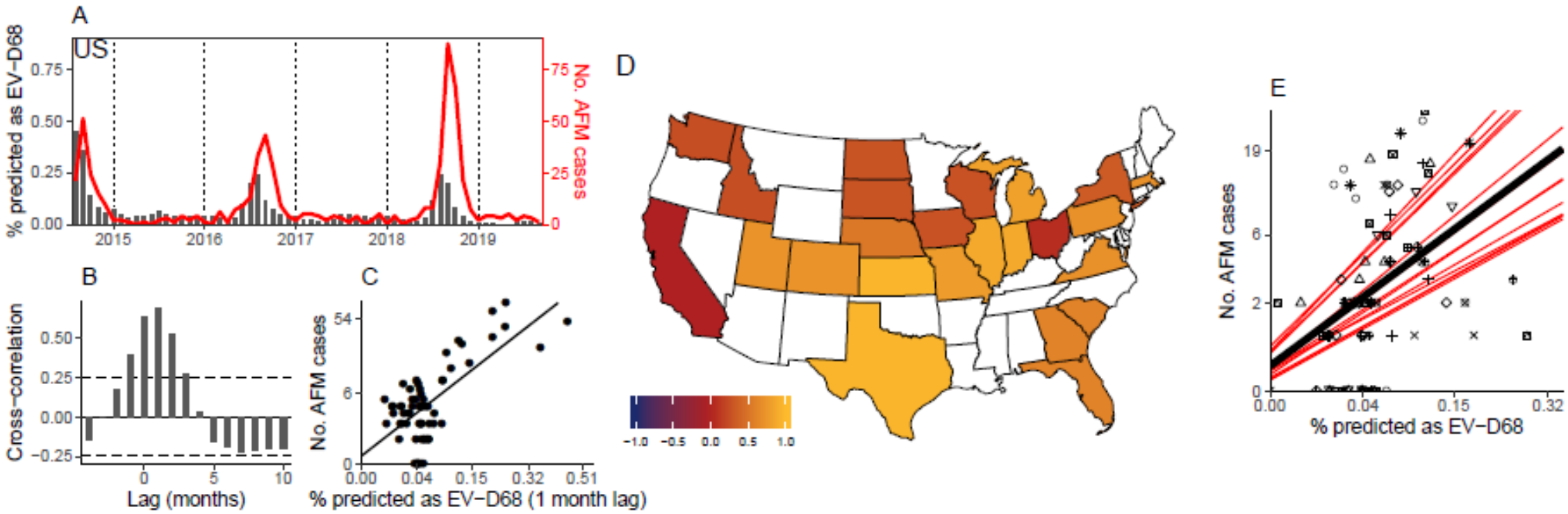
Temporal Association Between AFM Cases and EV-D68 Circulation in US





Messacar K, et al. (2019). "Acute Flaccid Myelitis Surveillance: A Signal Through the Noise" *Pediatrics.*
Messacar K, et al. (2019). "Continued Biennial Circulation of Enterovirus D68 in Colorado." *Journal of Clinical Virology.*

Epidemiologic Modeling: EV-D68 Driving AFM Seasonal Biennial Spikes in US



Park SW, Farrar J, Messacar K, Meyers L, Pons-Salort M, Grenfell BT. Epidemiological dynamics of enterovirus D68 in the US: implications for acute flaccid myelitis. *Science TM* 2021.

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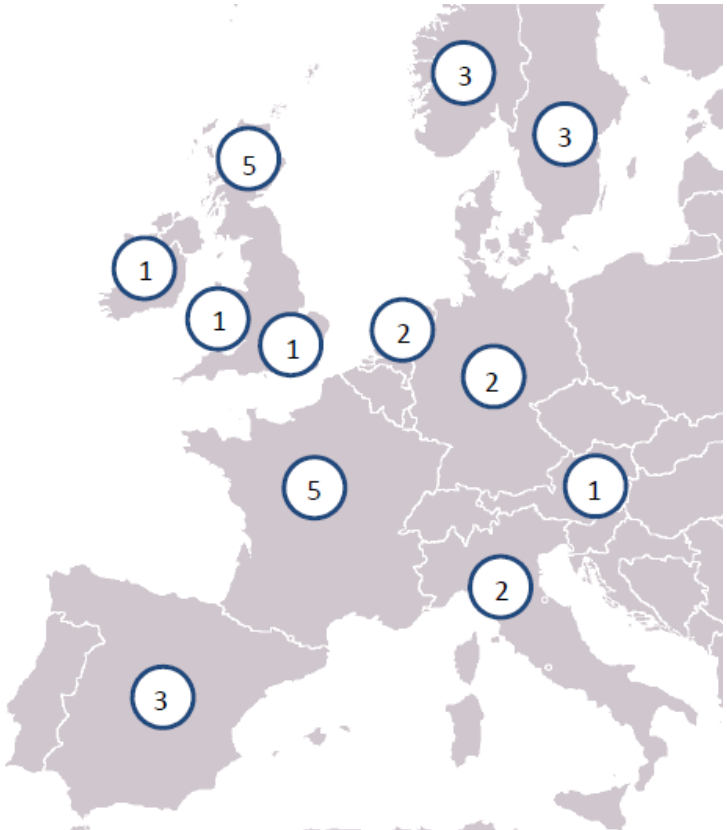
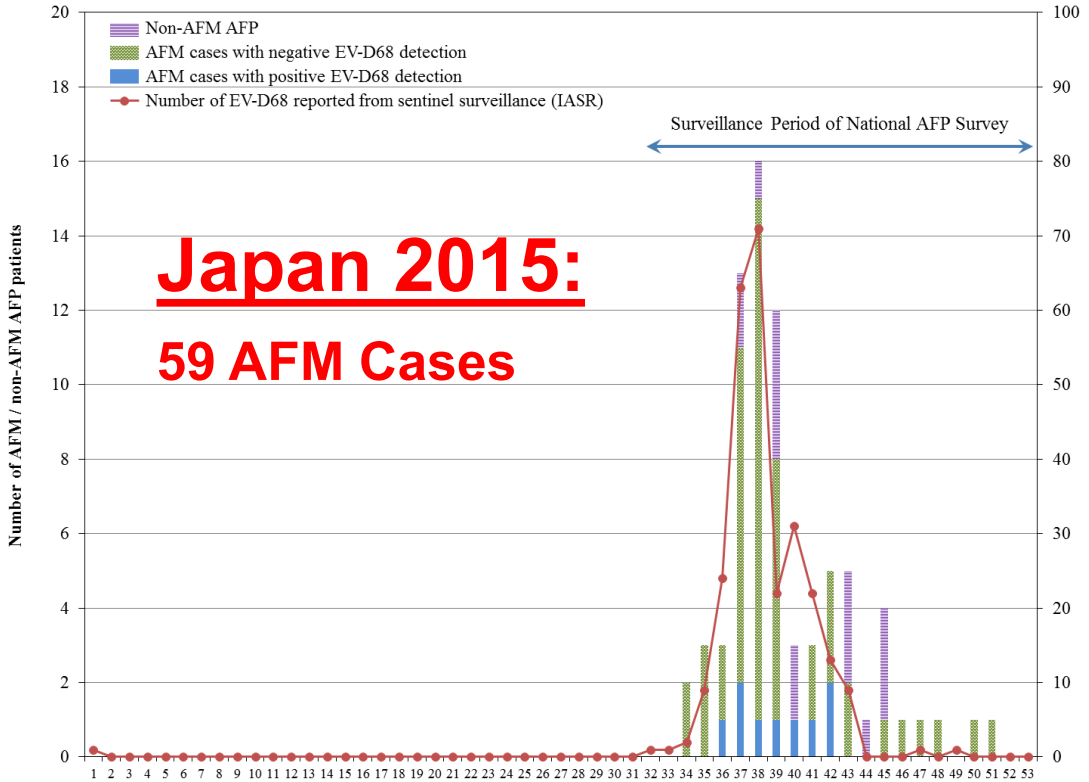
Global AFM Epidemiology

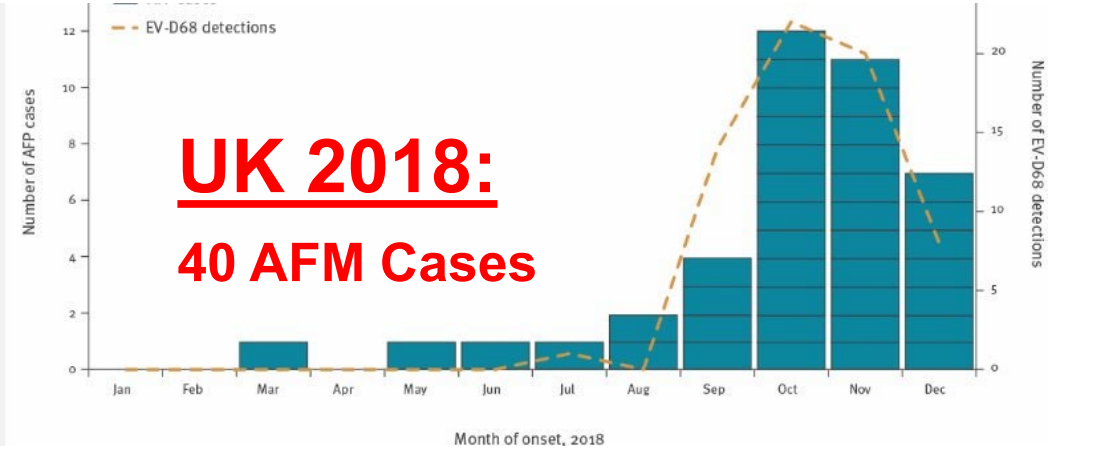
Twenty-nine Cases of Enterovirus-D68–associated Acute Flaccid Myelitis in Europe 2016

A Case Series and Epidemiologic Overview

Marjolein Knoester, MD, PhD, Jelte Helfferich, MD,† Randy Poelman, MSc,*
Coretta Van Leer-Buter, MD, PhD,* Oebele F. Brouwer, MD, PhD,† and Hubert G. M. Niesters, PhD,*
on Behalf of the 2016 EV-D68 AFM Working Group*





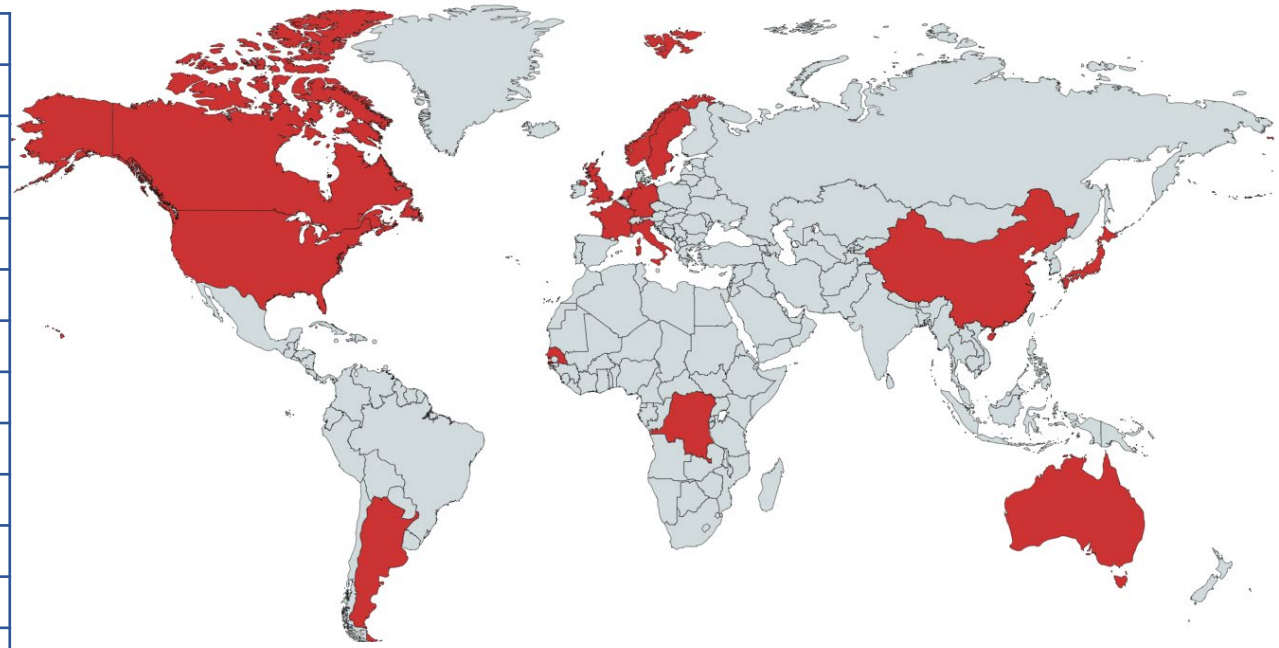


Chong, P. F., et al. (2017). "Clinical Features of Acute Flaccid Myelitis Temporally Associated with an Enterovirus D68 Outbreak: Results of a Nationwide Survey of Acute Flaccid Paralysis in Japan, August-December 2015." *Clin Infect Dis.*
The United Kingdom Acute Flaccid Paralysis Afp Task, F. (2019). "An increase in reports of acute flaccid paralysis (AFP) in the United Kingdom, 1 January 2018-21 January 2019: early findings." *Euro Surveill* ***24****(6).*

Global Recognition of EV-D68 AFM

Reported AFP/AFM Cases with EV-D68 in Biologic Specimens

Country	# Cases (Year of Presentation)
Argentina	4 (2016)
Australia	2 (2010)
Canada	7 (2014)
China	1 (2018)
Denmark	1 (2019)
DR Congo	1 (NR)
France	2 (2014), 5 (2016), 1 (2019)
Germany	2 (2016), 1 (2019)
United Kingdom	1 (2014), 2 (2015), 6 (2016), 9 (2018)
Italy	2 (2016)
Japan	3 (2013), 9 (2015), 1 (2017)
Netherlands	2 (2016)
Norway	2 (2014), 3 (2016)
Senegal	3 (2016)
Spain	1 (2015), 4 (2016), 1 (2017), 2 (2018)
Sweden	3 (2016)
United States	1 (2005), 1 (2008), 1 (2009), 4 (2012), 12 (2014), 22 (2016), 30 (2018)

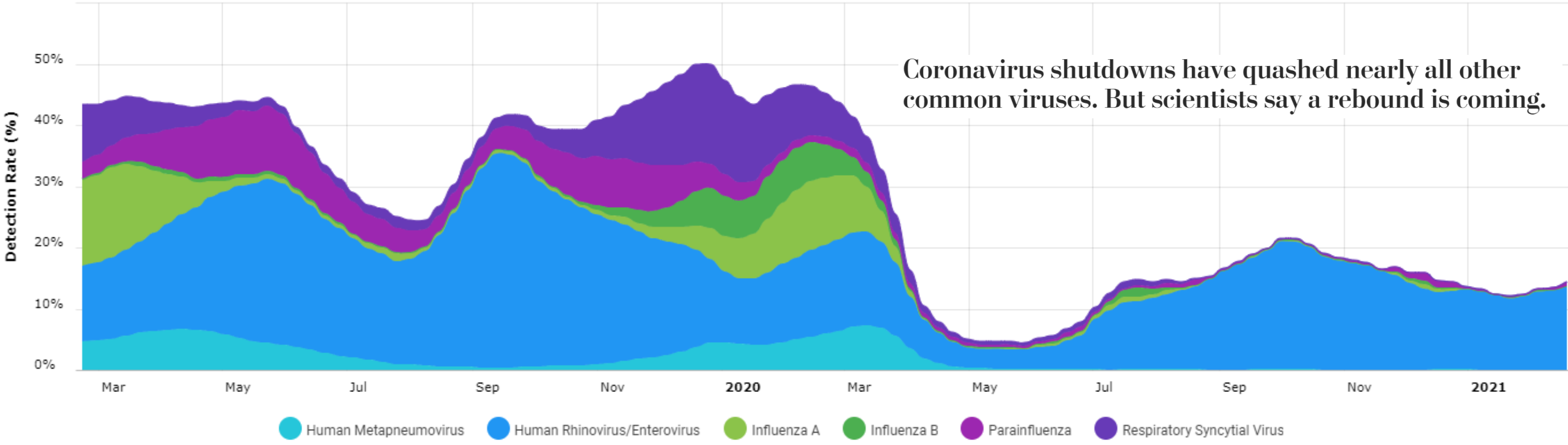


- **>150 cases in 20 countries on 6 continents**

Messacar, K., et al. (2018). "Enterovirus D68 and acute flaccid myelitis-evaluating the evidence for causality." *Lancet Infect Dis*.
Updated with new reported cases since publication

What Happened in 2020?

What Will Happen in 2020 and Beyond?



https://www.cdc.gov/acute-flaccid-myelitis/cases-in-us.html (accessed 2/18/21)

Park SW, Farrar J, Messacar K, Meyers L, Pons-Salort M, Grenfell BT. Epidemiological dynamics of enterovirus D68 in the US: implications for acute flaccid myelitis. *Science TM* 2021.

https://syndromictrends.com/metric/panel/rp/percent_positivity/organism/main (accessed 2/18/21)

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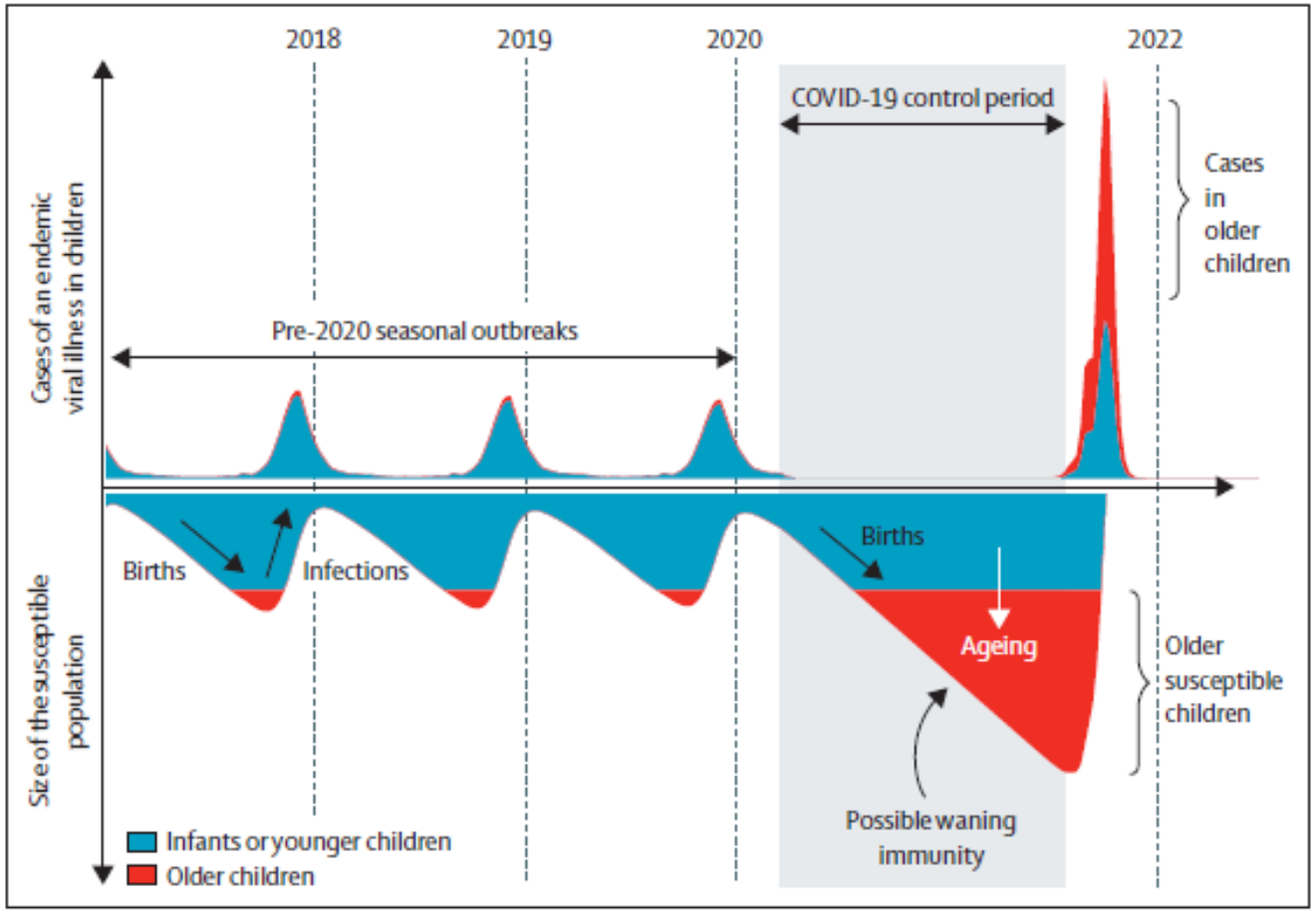
Advances in Preparedness: Epidemiologic Modeling



Messacar K, Baker RE, Park SW, Nguyen-Tran H, Cataldi JR, Grenfell B. Preparing for uncertainty: endemic paediatric viral illnesses after COVID-19 pandemic disruption. *The Lancet* 2022.

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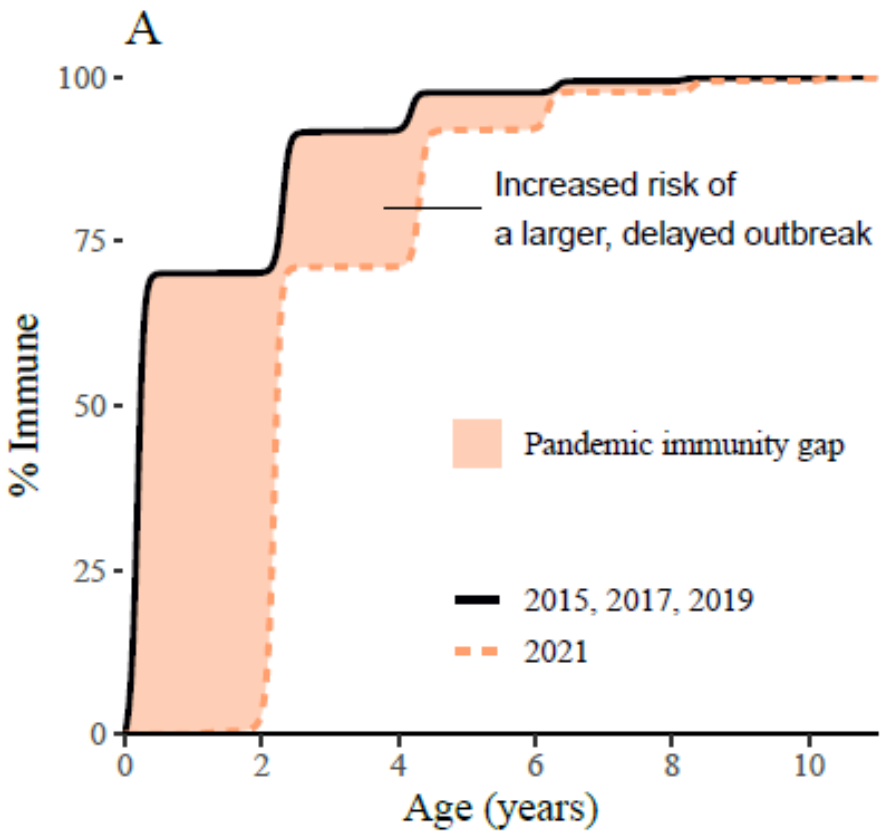
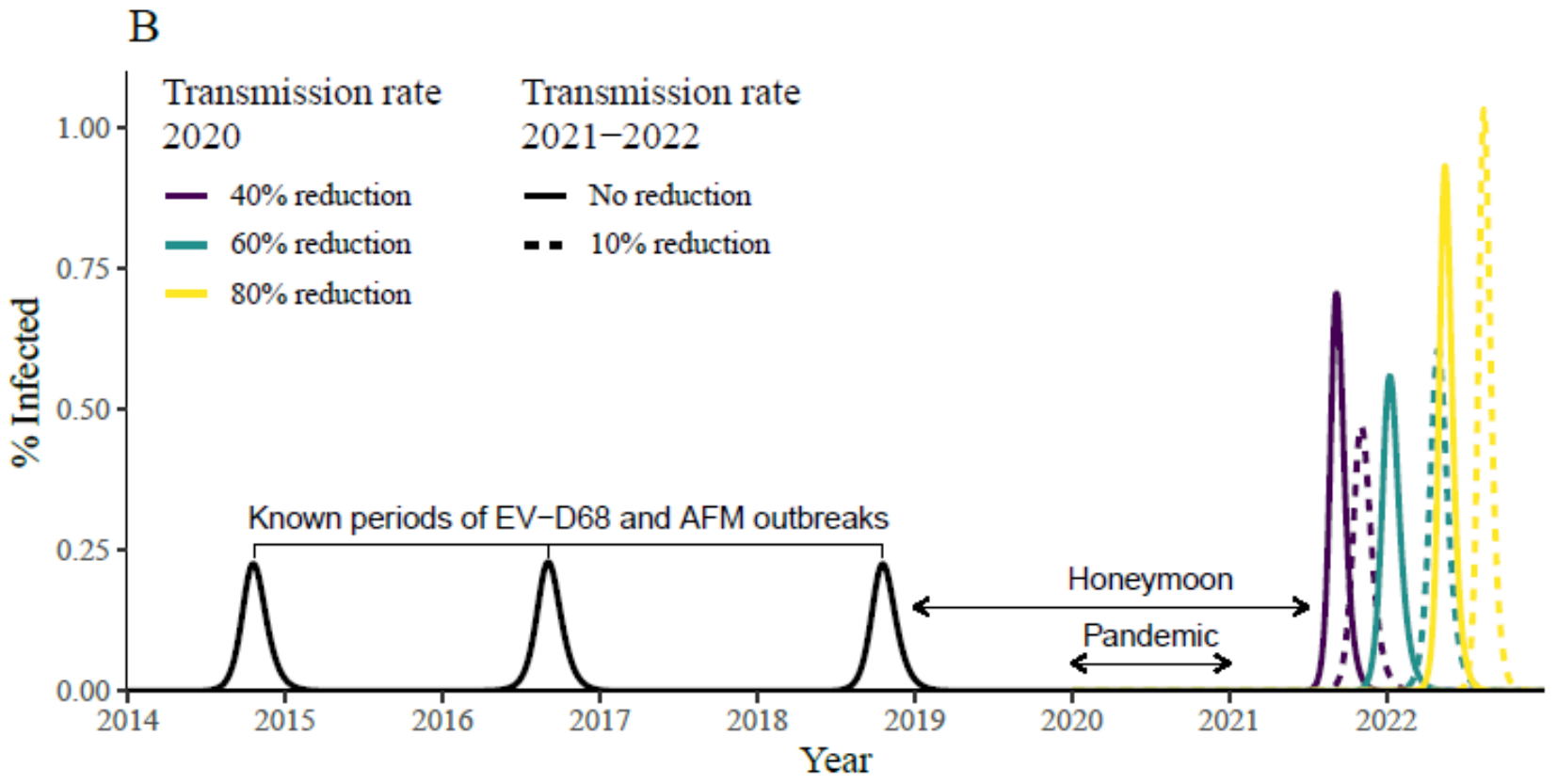
Advances in Preparedness: Epidemiologic Modeling





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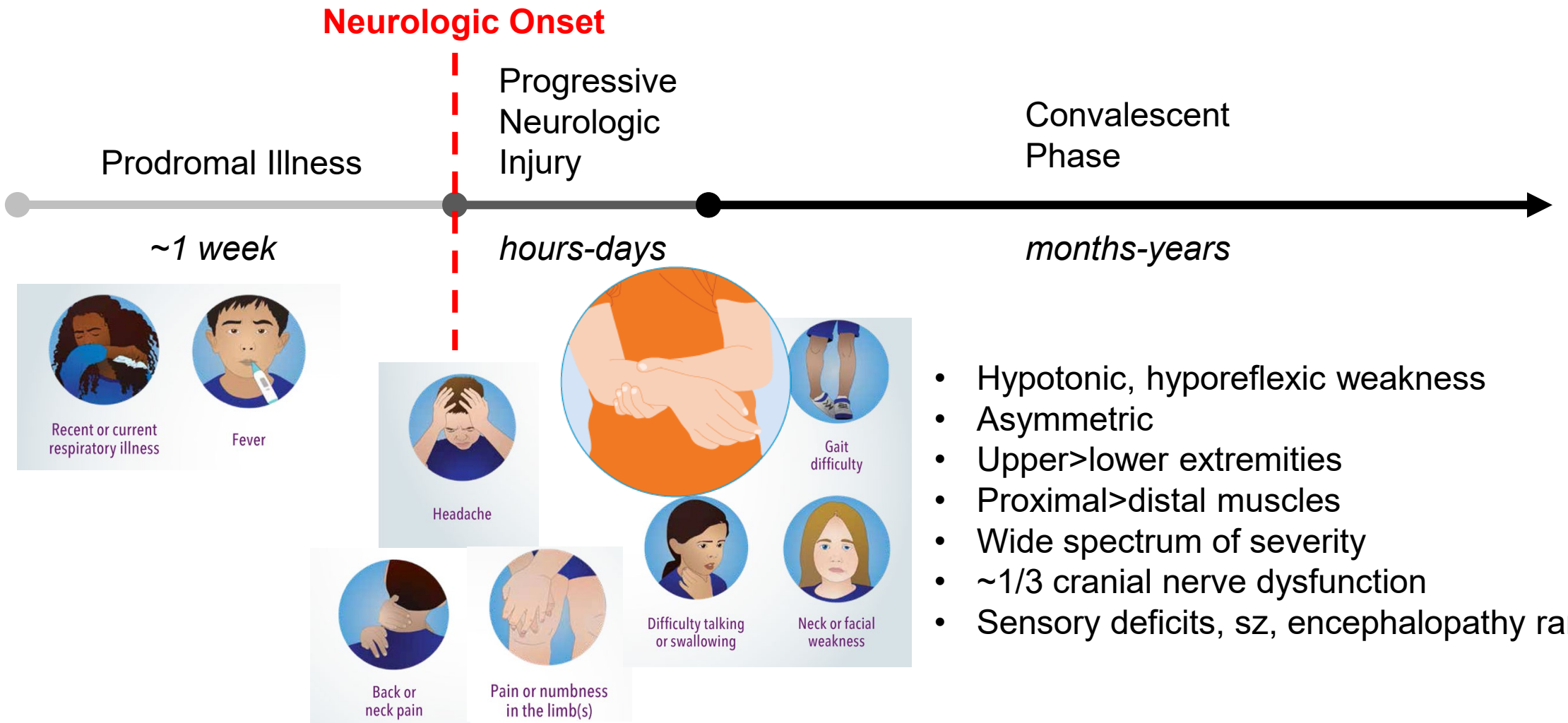
Nguyen-Tran H, Park SW, Messacar K, et al. Enterovirus D68: a test case for the use of immunological surveillance to develop tools to mitigate the pandemic potential of emerging pathogens. *Lancet Microbe* 2022.

AFM Natural History



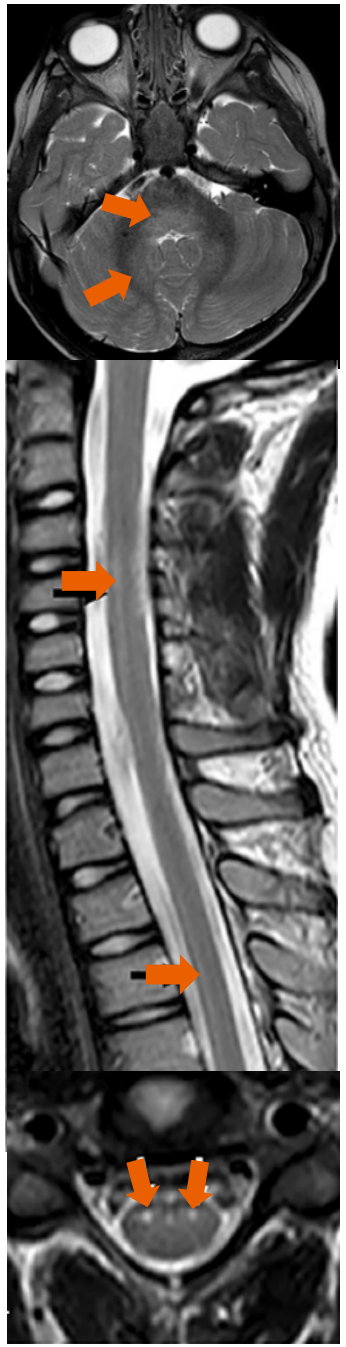
- Hypotonic, hyporeflexic weakness
- Asymmetric
- Upper>lower extremities
- Proximal>distal muscles
- Wide spectrum of severity
- ~1/3 cranial nerve dysfunction
- Sensory deficits, sz, encephalopathy rare

Messacar, K., et al. (2016). "Acute flaccid myelitis: A clinical review of US cases 2012-2015." Ann Neurol **80**(3): 326-338.

AFM Diagnosis

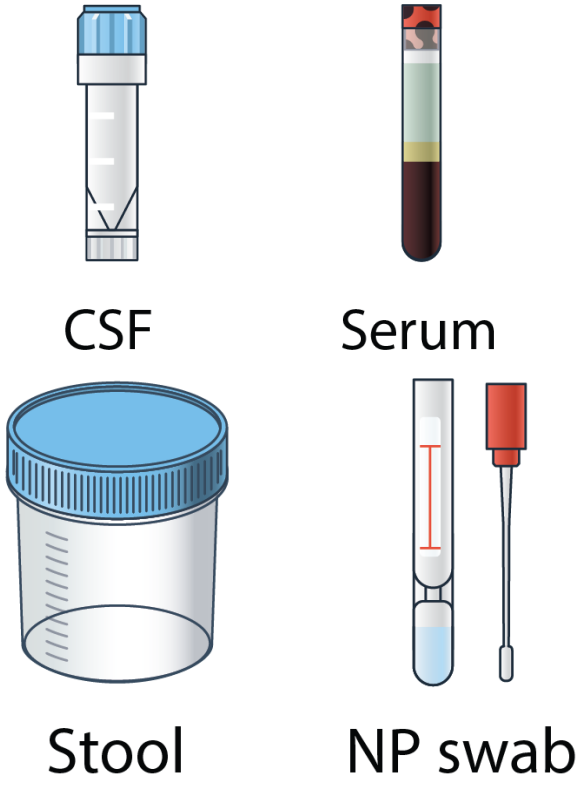
AFM Diagnostic Studies

- **Neurologic exam:** flaccid weakness
- **Brain/spinal cord MRI:** longitudinal gray matter +/- brainstem lesions
- **Lumbar puncture:** CSF pleocytosis



AFM Etiologic Evaluation

- **Early biological specimen collection**



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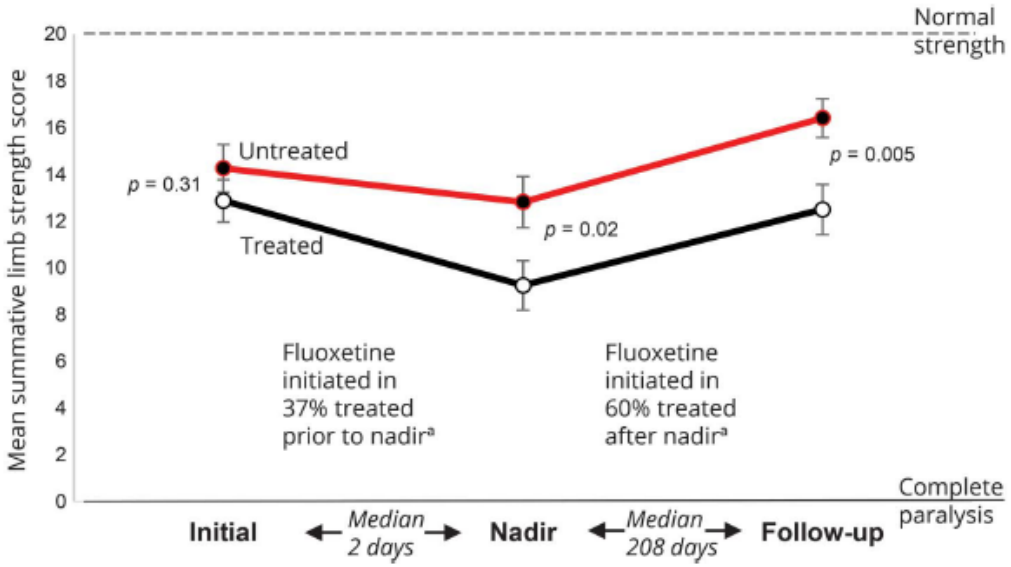
Hopkins SE, Elrick MJ, Messacar K. Acute Flaccid Myelitis-Keys to Diagnosis, Questions About Treatment, and Future Directions. JAMA pediatrics 2018.
https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinicians-health-departments.html

AFM: Treatment

- No controlled studies of treatment efficacy in humans
  - Immunomodulatory therapies commonly administered
    - **IVIG:** high neutralizing Ab titers to EV-D68
      - Monoclonal EV-D68 Abs created, undergoing testing
    - **Steroids:** recommended when spinal cord edema→UMN signs due to compression
    - **Antivirals:** No available anti-EV medications
      - Polio antivirals in dev't with EV-D68, EV-A71 activity



- 2016: Fluoxetine administered off-label due to *in vitro* EV-D68 activity
  - No signal of efficacy in retrospective analysis of limb strength outcomes in tx'd (n=26) vs. untx'd (n=26)

Zhang Y, Moore DD, Nix WA, Oberste MS, Weldon WC. Neutralization of Enterovirus D68 isolated from the 2014 US outbreak by commercial IVIG products. JCV 2015;69:172-175

Messacar, K., et al. (2018). "Safety, tolerability, and efficacy of fluoxetine as an antiviral for acute flaccid myelitis." Neurology.

AFM Therapies: Supportive Care

- Hospitalize all suspected cases presenting in the acute phase
- Monitor respiratory status
  - Ability to protect airway
  - Negative inspiratory flow
  - ➢Intubation, ventilation for respiratory failure
- Monitor for constipation, urinary retention
  - ➢Bowel regimen, catheterization
- Support hydration/nutrition
  - ➢Enteral feeding


Review

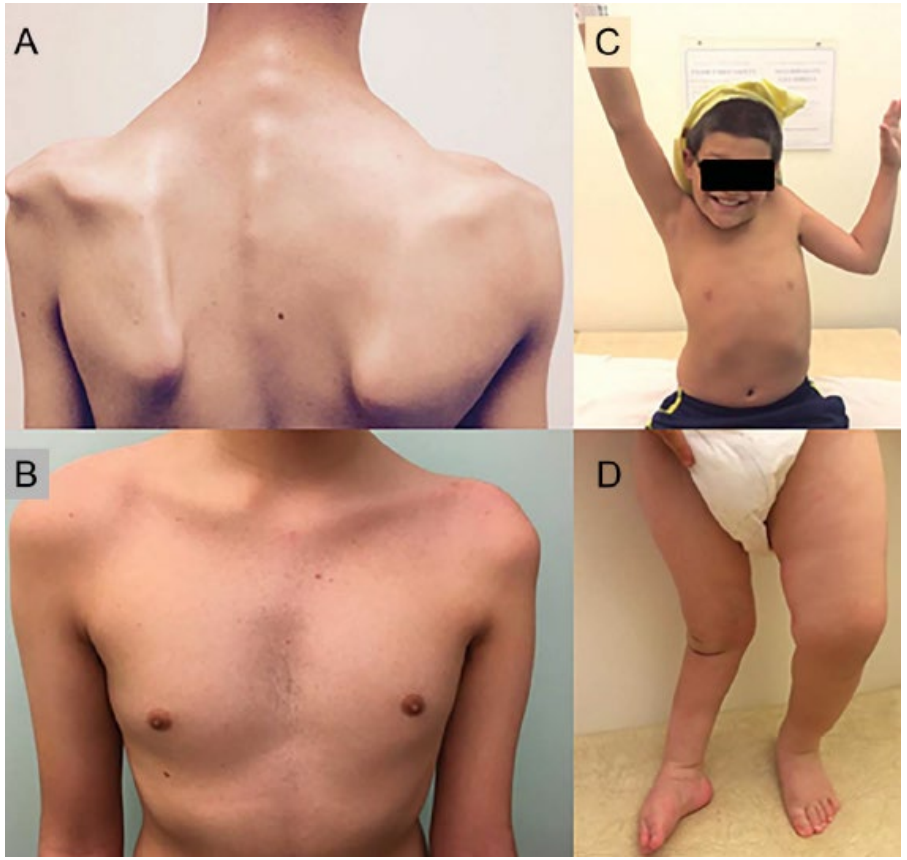
Acute flaccid myelitis: cause, diagnosis, and management

Olwen C Murphy, Kevin Messacar, Leslie Benson, Riley Bove, Jessica L Carpenter, Thomas Crawford, Janet Dean, Roberta DeBiasi, Jay Desai, Matthew J Elrick, Raquel Farias-Moeller, Grace Y Gombolay, Benjamin Greenberg, Matthew Harmelink, Sue Hong, Sarah E Hopkins, Joyce Oleszek, Catherine Otten, Cristina L Sadowsky, Teri L Schreiner, Kiran T Thakur, Keith Van Haren, Carolina M Carballo, Pin Fee Chong, Amary Fall, Vykuntaraju K Gowda, Jelte Helfferich, Ryutaro Kira, Ming Lim, Eduardo L Lopez, Elizabeth M Wells, E Ann Yeh, Carlos A Pardo; on behalf of the AFM working group*

Murphy OC, Messacar K, Benson L, et al. Acute flaccid myelitis: cause, diagnosis, and management. *Lancet* 2021; 397(10271): 334-46.

AFM: Outcomes

- Functional improvements with rehabilitation therapies
  - Distal, less-affected muscles > proximal, more-affected muscles > completely denervated muscles
- Most recovery occurs early
  - Improvement still noted >12 mos
- Motor deficits persist in ~75%
  - Few completely recover



Polio-like muscle atrophy in affected limbs

Martin, J. A., et al. (2017). "Outcomes of Colorado children with acute flaccid myelitis at 1 year." Neurology **89**(2): 129-137.
Yea, C., et al. (2017). "Longitudinal Outcomes in the 2014 Acute Flaccid Paralysis Cluster in Canada." J Child Neurol **32**(3): 301-307.
Gordon-Lipkin, E., et al. (2018). "Comparative quantitative clinical, neuroimaging, and functional profiles in children with acute flaccid myelitis at acute and convalescent stages of disease." Dev Med Child Neurol.

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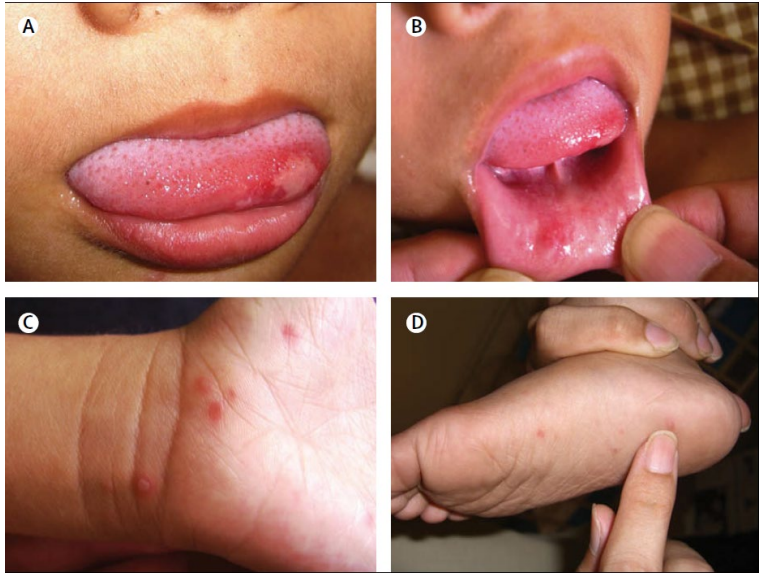
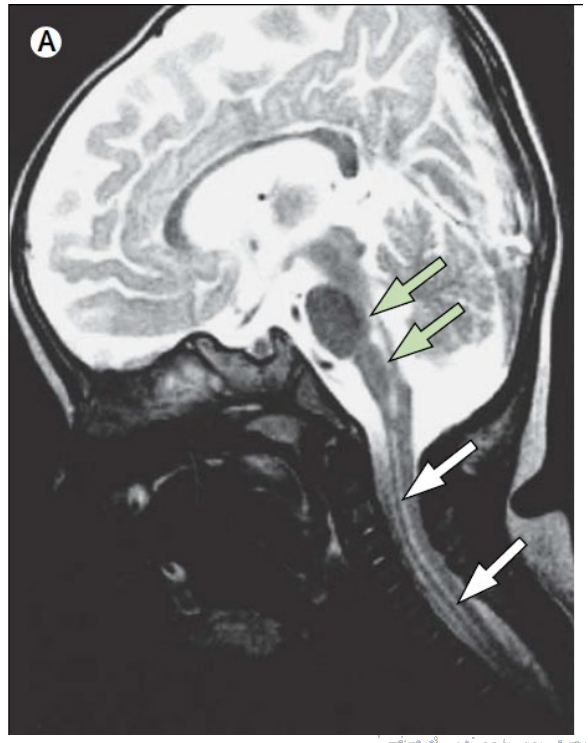
Enterovirus A71 Myelitis



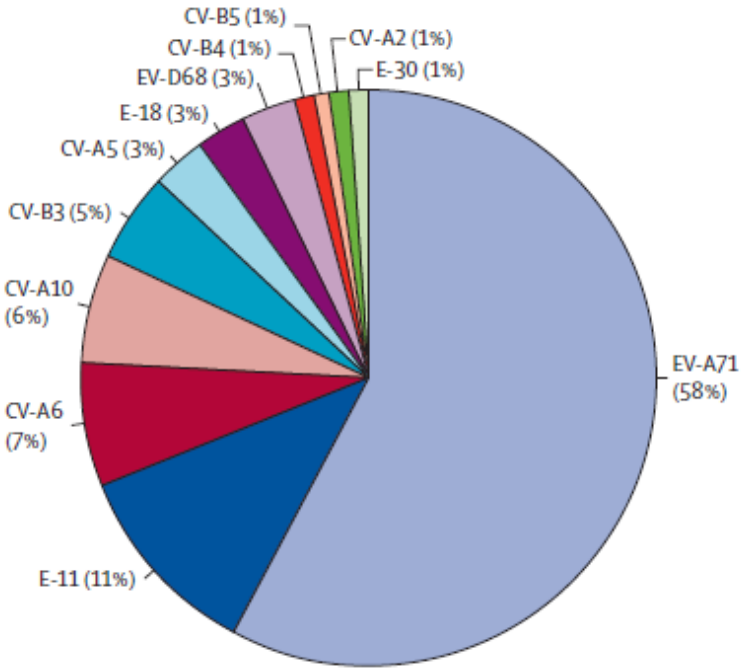
- Hand-foot-mouth disease outbreaks
- Brainstem encephalitis→noncardiogenic pulmonary edema
- Myelitis→flaccid limb weakness, meeting AFM case definition
- 1970s- : sporadic epidemics in N. America, Europe, Africa, Australia; now every 2-5 year epidemics in Asia-Pacific region
  - Ex: Taiwan 1998: 1.5 million infected, 405 with neuro ds
- Notable recent European outbreaks in France (2016), Spain (2017), and Germany (2019)

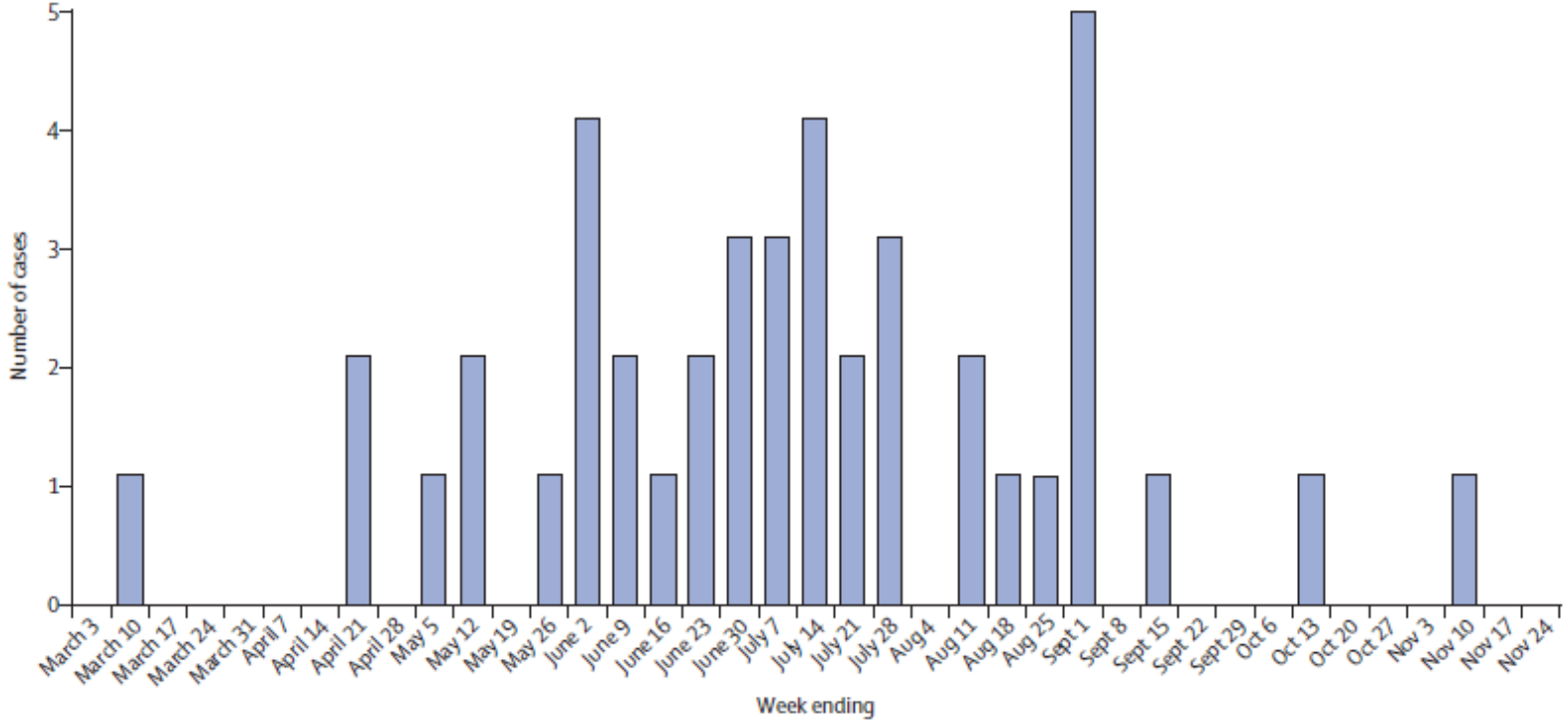


Ooi, M. H., et al. (2010). "Clinical features, diagnosis, and management of enterovirus 71." The Lancet Neurology 9(11): 1097-1105.
Solomon, T., et al. (2010). "Virology, epidemiology, pathogenesis, and control of enterovirus 71." Lancet Infect Dis 10(11): 778-790.
Hu, Y., et al. (2015). "Clinical Analysis of 134 Children with Nervous System Damage Caused by Enterovirus 71 Infection." Pediatr Infect Dis J 34(7): 718-723.
Casas-Alba D, et al. Outbreak of brainstem encephalitis associated with enterovirus-A71 in Catalonia, Spain (2016): a clinical observational study in a children's reference centre in Catalonia. Clin Microbiol Infect 2017; 23(11): 874-81.
Antona D et al. Severe paediatric conditions linked with EV-A71 and EV-D68, France, May to October 2016. Euro surveillance 2016; 21(46).
Bottcher S, et al.. Increased detection of enterovirus A71 infections, Germany, 2019. Euro surveillance : 2019; 24(39).

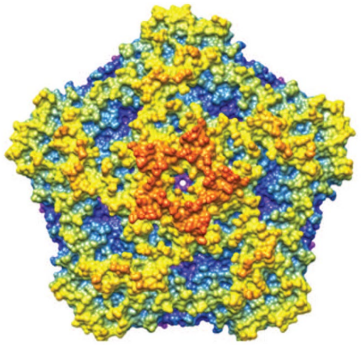
2018: Outbreak of EV-A71 Neurologic Disease in CO Children

- May 2018: Increase in EV-associated neurologic cases
  - Specimens typed at EV-A71 at CDC
- N=43 cases of EV-A71 neurologic disease, including 10 AFM cases





Messacar K, Spence-Davizon E, Osborne C, et al. Clinical characteristics of enterovirus A71 neurological disease during an outbreak in children in Colorado, USA, in 2018: an observational cohort study. *Lancet Infect Dis.* 2019.



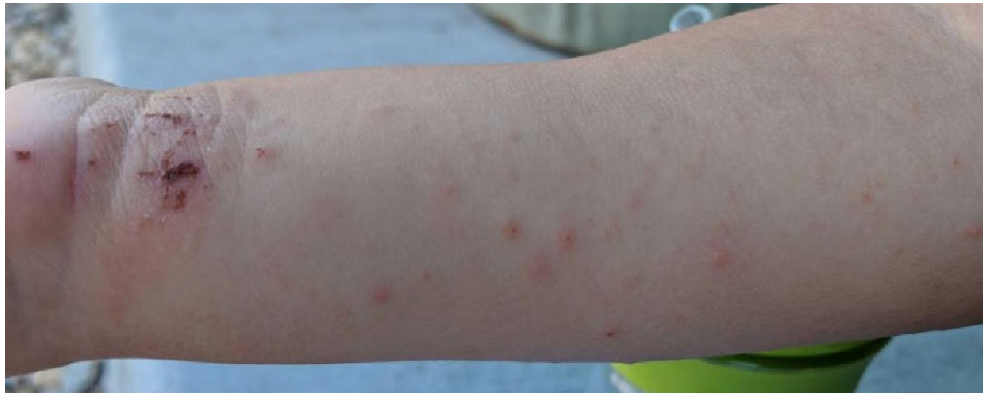
Not All AFM is the Same:
Differing AFM Phenotype by Etiology

EV-D68 Associated AFM Cases

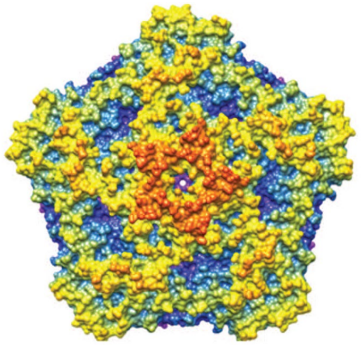
- Respiratory prodrome

EV-A71 Associated AFM Cases

- Fever, ~1/2 HFMD prodrome



Messacar K, Spence-Davizon E, Osborne C, et al. Clinical characteristics of enterovirus A71 neurological disease during an outbreak in children in Colorado, USA, in 2018: an observational cohort study. *Lancet Infect Dis.* 2019.



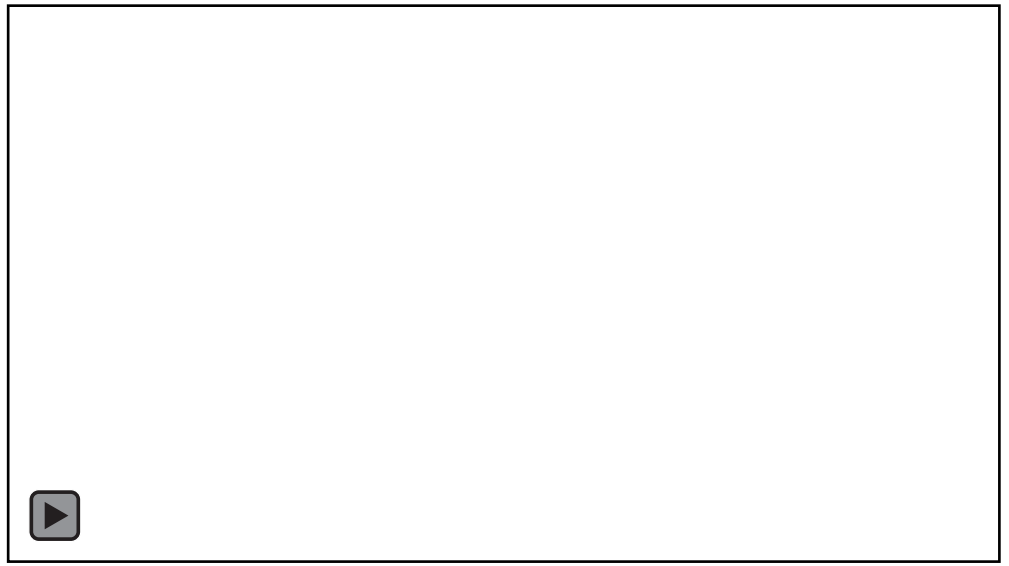
Not All AFM is the Same:
Differing AFM Phenotype by Etiology

EV-D68 Associated AFM Cases

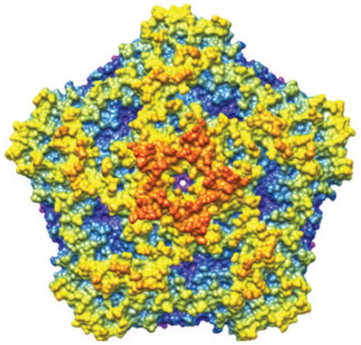
- Respiratory prodrome
- Limb weakness +/- CN dysfcn

EV-A71 Associated AFM Cases

- Fever, ~1/2 HFMD prodrome
- +myoclonus, ataxia, autonomic sx



Messacar K, Spence-Davizon E, Osborne C, et al. Clinical characteristics of enterovirus A71 neurological disease during an outbreak in children in Colorado, USA, in 2018: an observational cohort study. *Lancet Infect Dis.* 2019.



Not All AFM is the Same:
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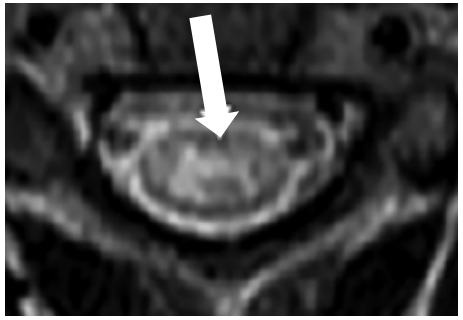
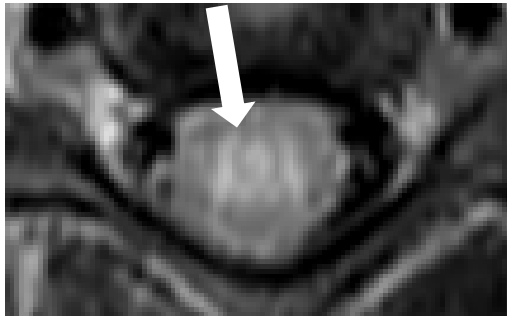
EV-D68 Associated AFM Cases

- Respiratory prodrome
- Limb weakness +/- CN dysfcn
- Gray matter-predom myelitis

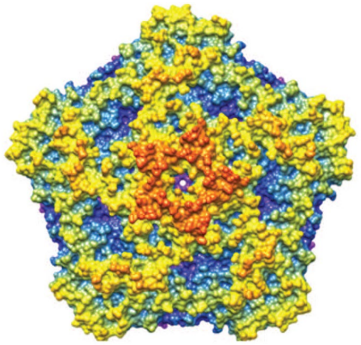
EV-A71 Associated AFM Cases

- Fever, ~1/2 HFMD prodrome
- +myoclonus, ataxia, autonomic sx
- Indistinguishable from EV-D68





Messacar K, Spence-Davizon E, Osborne C, et al. Clinical characteristics of enterovirus A71 neurological disease during an outbreak in children in Colorado, USA, in 2018: an observational cohort study. *Lancet Infect Dis.* 2019.



Not All AFM is the Same:
Differing AFM Phenotype by Etiology

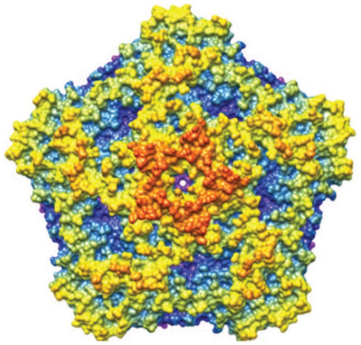
EV-D68 Associated AFM Cases

- Respiratory prodrome
- Limb weakness +/- CN dysfcn
- Gray matter-predom myelitis
- ↑ detection in NP specimens

EV-A71 Associated AFM Cases

- Fever, ~1/2 HFMD prodrome
- +myoclonus, ataxia, autonomic sx
- Indistinguishable from EV-D68
- Detected in rectal/stool>OP>NP

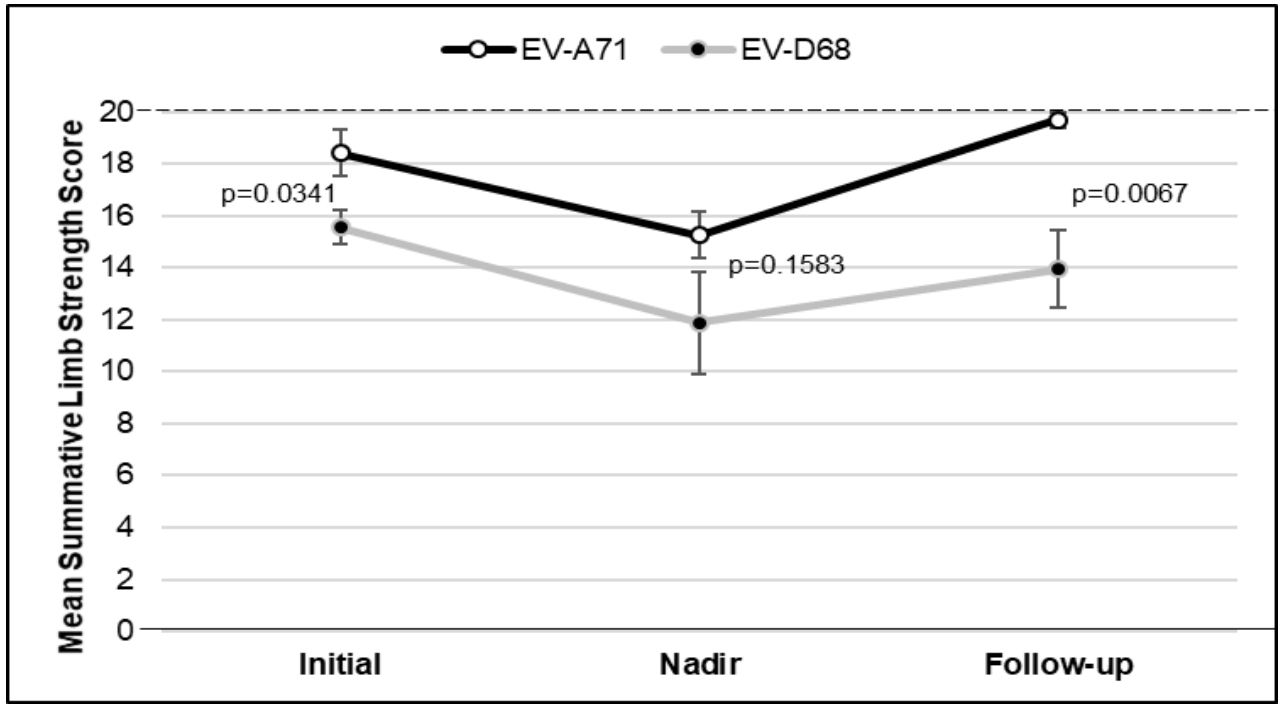
Messacar K, Spence-Davizon E, Osborne C, et al. Clinical characteristics of enterovirus A71 neurological disease during an outbreak in children in Colorado, USA, in 2018: an observational cohort study. *Lancet Infect Dis.* 2019.



Not All AFM is the Same:
Differing AFM Phenotype by Etiology

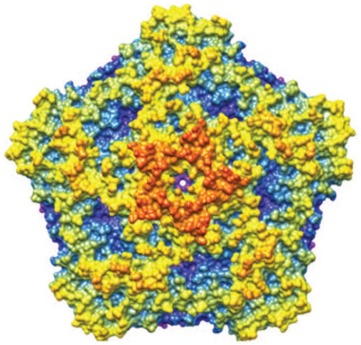
EV-D68 Associated AFM Cases

EV-A71 Associated AFM Cases

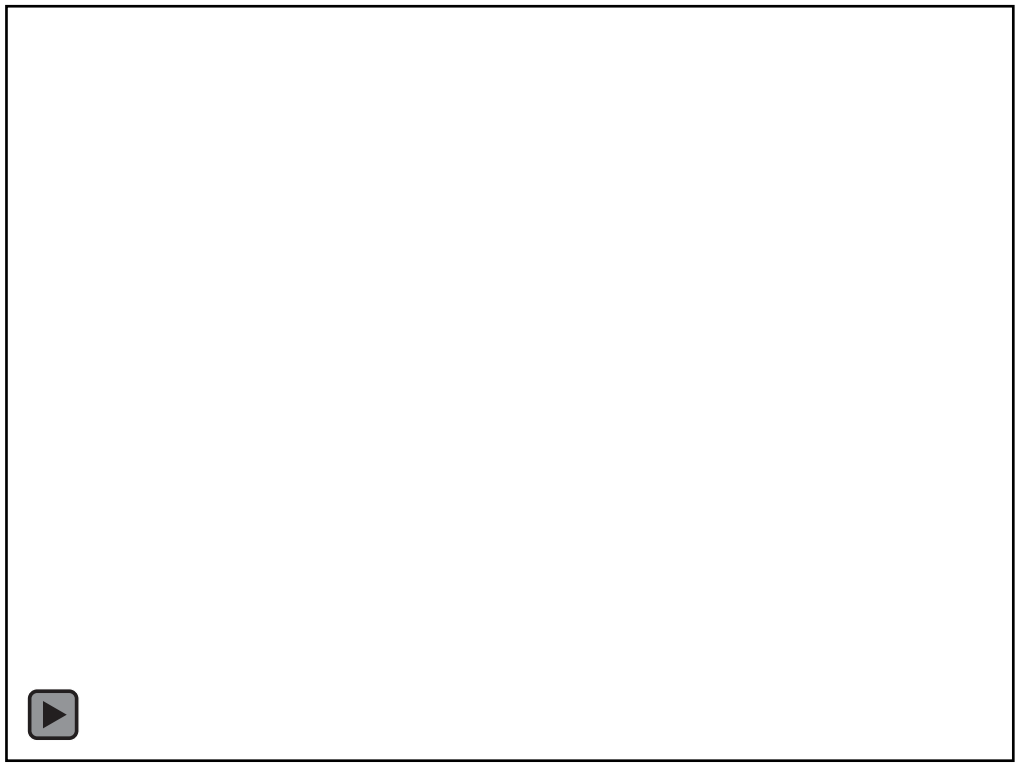


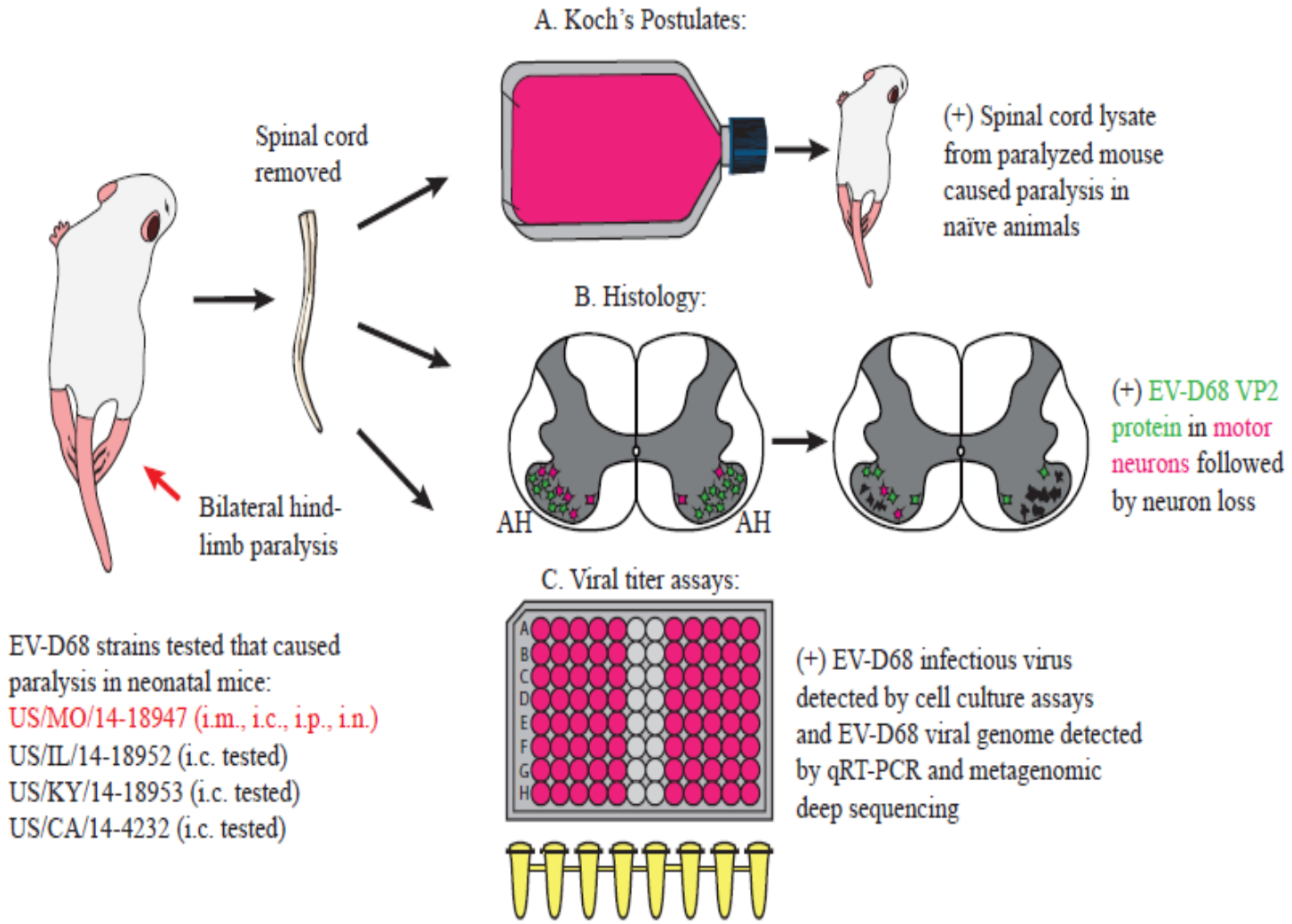
- Majority: persistent weakness
- Majority: complete recovery

Messacar K, Spence-Davizon E, Osborne C, et al. Clinical characteristics of enterovirus A71 neurological disease during an outbreak in children in Colorado, USA, in 2018: an observational cohort study. *Lancet Infect Dis.* 2019.



AFM Pathophysiology:
EV-D68 Causes AFM in Mice

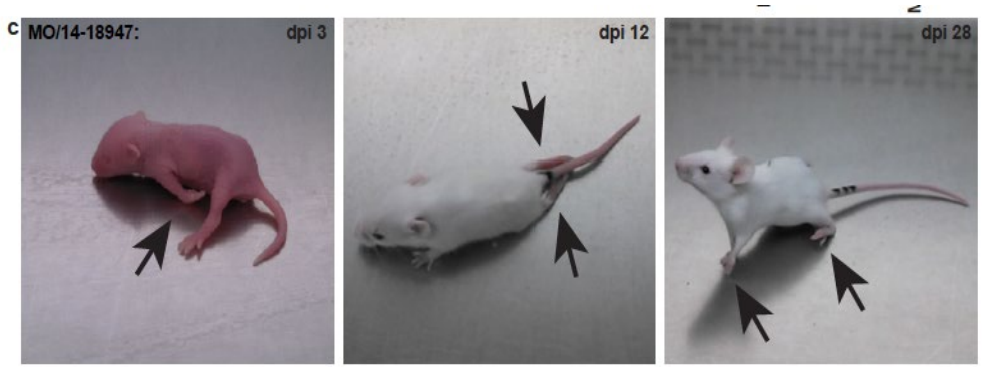




EV-D68 strains tested that caused paralysis in neonatal mice:
US/MO/14-18947 (i.m., i.c., i.p., i.n.)
US/IL/14-18952 (i.c. tested)
US/KY/14-18953 (i.c. tested)
US/CA/14-4232 (i.c. tested)

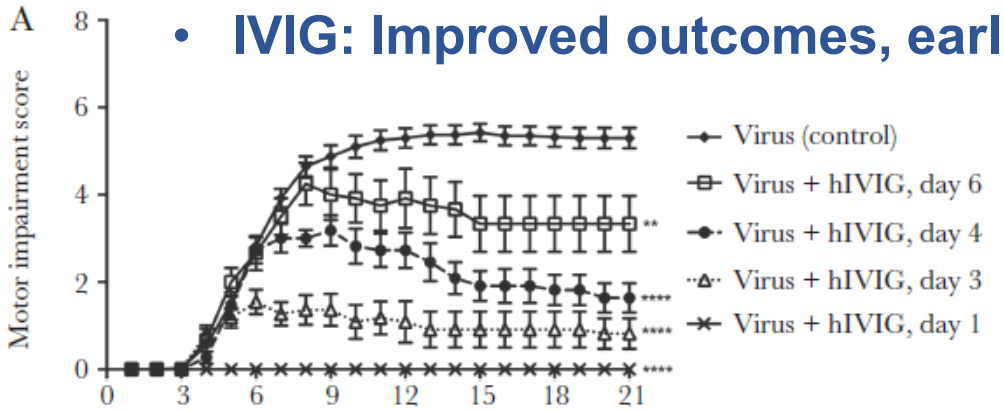
Hixon, A. M., et al. (2017). "A mouse model of paralytic myelitis caused by enterovirus D68." PLoS Pathog **13**(2): e1006199.
Messacar K AE, Hixon AM, Leer-Buter CV, et al.. Enterovirus D68 and Acute Flaccid Myelitis—Evaluating the Evidence for Causality. *The Lancet Infectious diseases*. 2018.

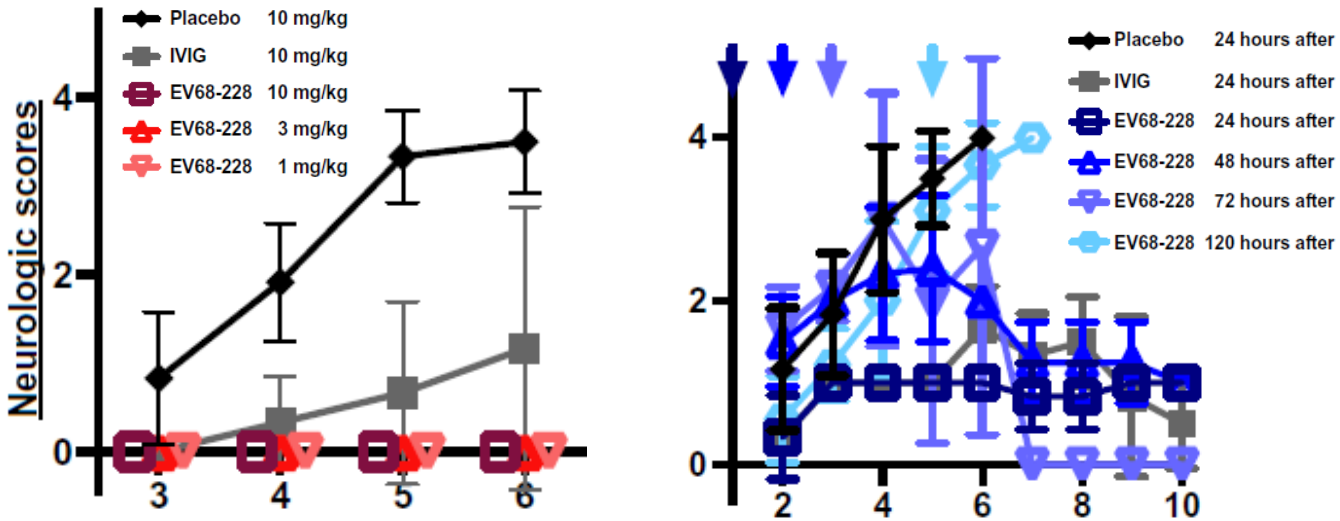
Research Advances in AFM Tx: Mouse Model Treatment Efficacy



- Fluoxetine: No effect
- Steroids: Increased viral titers in spinal cord, worsened motor impairment, increased mortality

- **IVIG: Improved outcomes, earlier better**

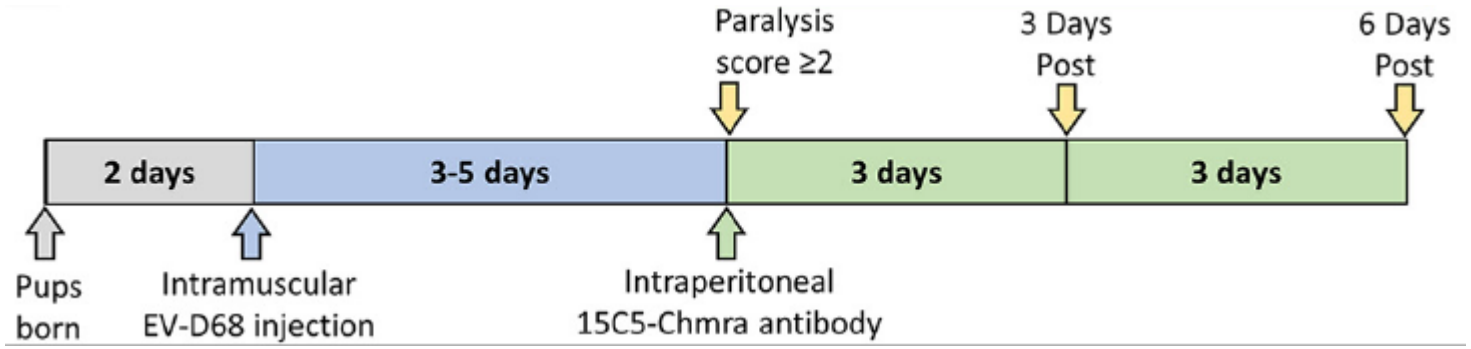


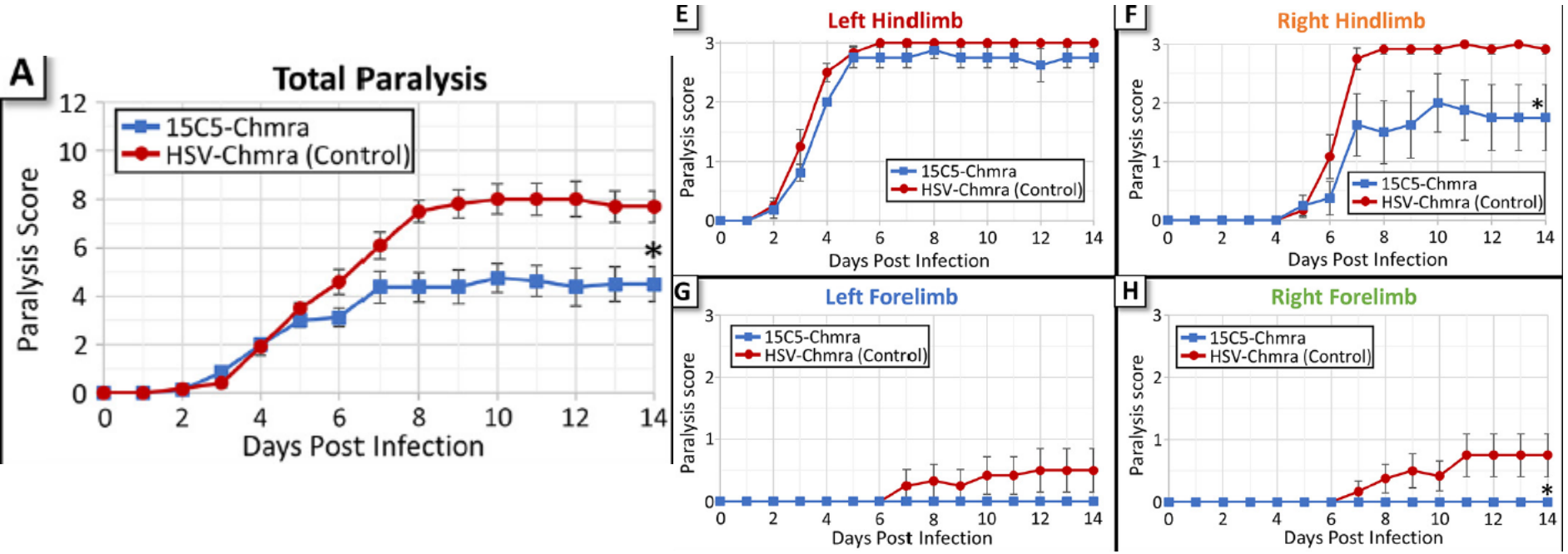


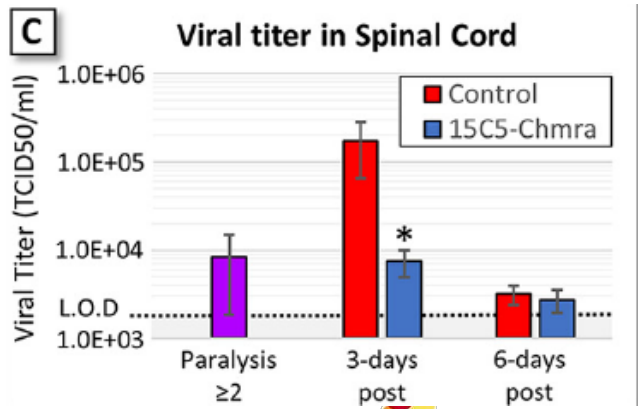
- **Monoclonal EV-D68 Ab: Improved outcomes>IVIG, even out to 48-72 hrs post**

Hixon, A. M., et al. (2017). "Evaluating treatment efficacy in a mouse model of enterovirus D68 paralytic myelitis." J Infect Dis.
Vogt MR, Fu J, Kose N, et al. Human antibodies neutralize enterovirus D68 and protect against infection and paralytic disease. Sci Immunol 2020; 5(49).

Advances in Treatment:
Mouse Model Treatment Efficacy







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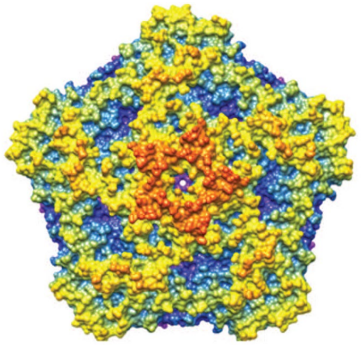
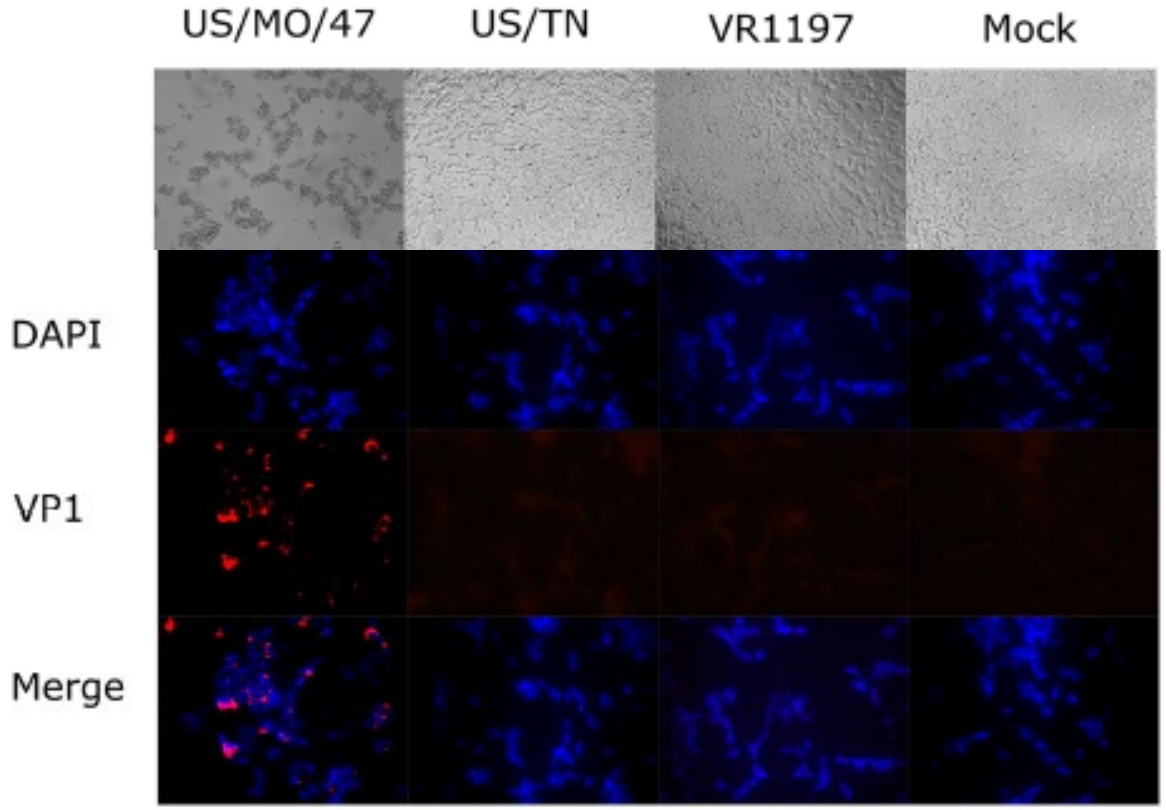
Rudy MJ, Frost J, Clarke P, Tyler KL. "Neutralizing Antibody Given after Paralysis Onset Reduces the Severity of Paralysis Compared to Nonspecific Antibody-Treated Controls in a Mouse Model of EV-D68-Associated Acute Flaccid Myelitis" *Antimicrobial Agents and Chemotherapy* (2022, ahead of print)

University of Colorado Anschutz Medical Campus School of Medicine



AFM Pathophysiology:
EV-D68 Infects Neurons



Neuroblastoma-derived
SH-SY5Y neuronal cell line

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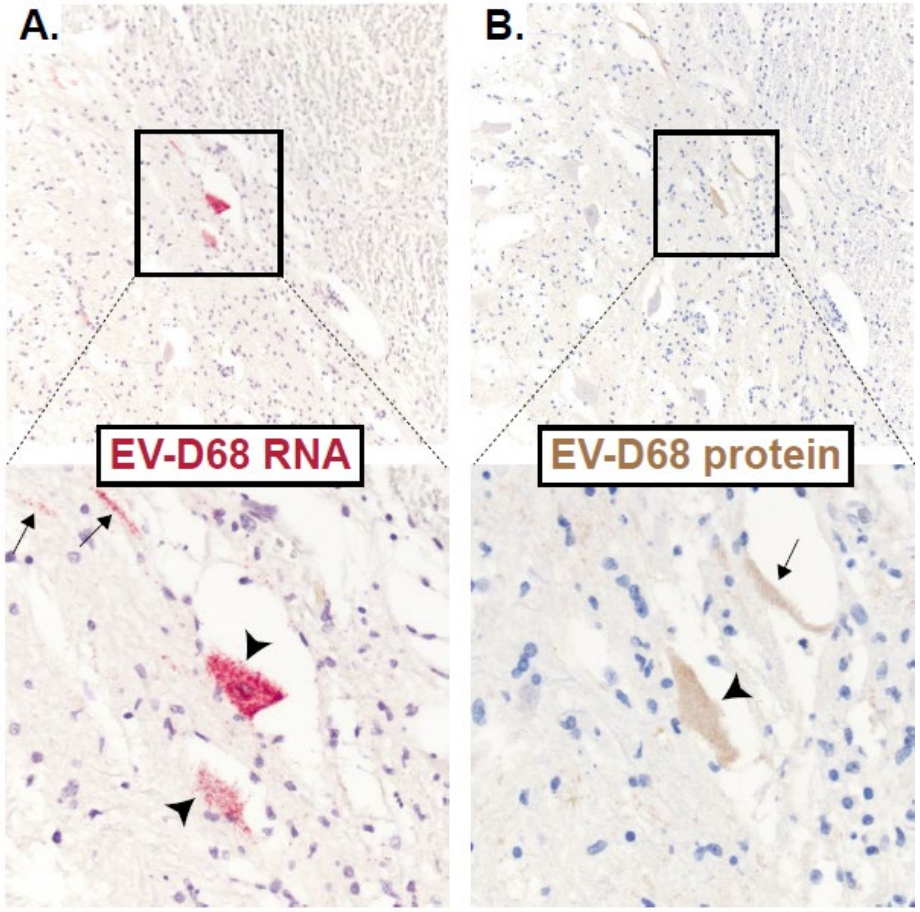
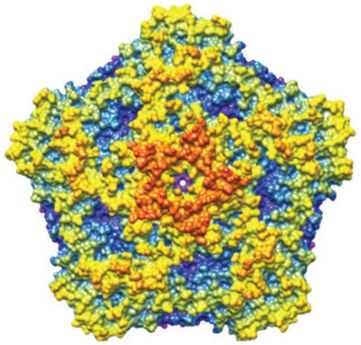
Brown DM, Hixon AM, Oldfield LM, et al. Contemporary Circulating Enterovirus D68 Strains Have Acquired the Capacity for Viral Entry and Replication in Human Neuronal Cells. MBio. 2018;9(5).

Advances in Pathophysiology:
EV-D68 infects spinal cord motor neurons in human AFM

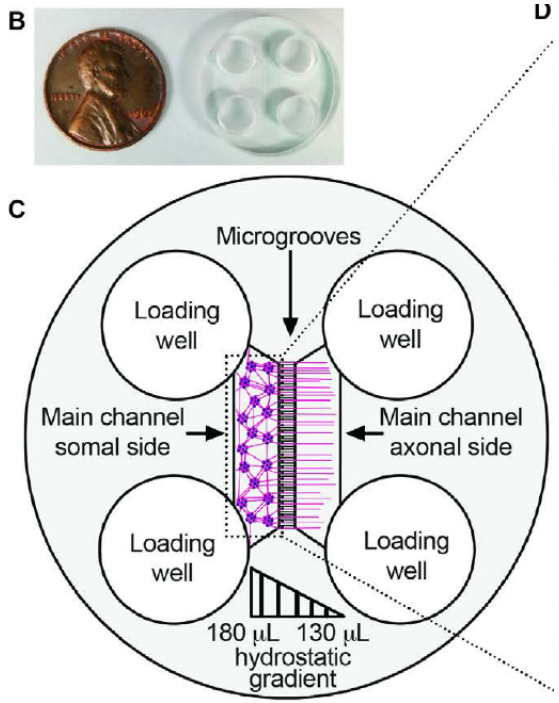


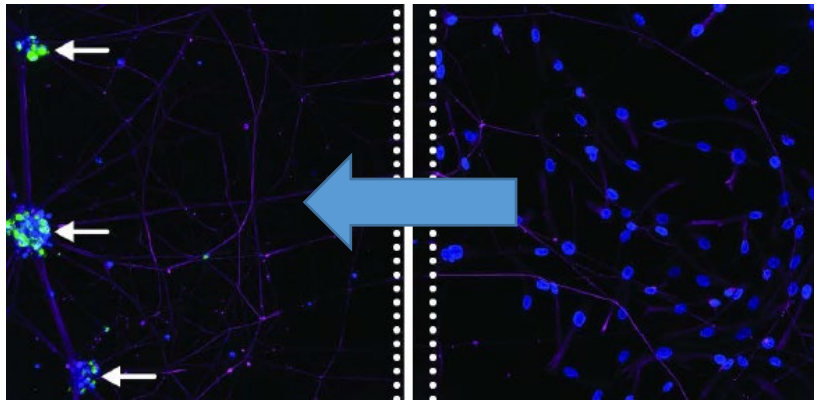
- Fall 2008: 5yo boy developed flaccid paralysis and respiratory failure following nonspecific viral illness
- Autopsy findings demonstrated T-lymphocyte inflammation in anterior spinal cord and neuronophagia
  - CSF +EV-D68 by PCR
- Subsequent analysis stained EV-D68 RNA and protein in anterior horn motor neurons of spinal cord

Kreuter JD, Barnes A, McCarthy JE, et al. A fatal central nervous system enterovirus 68 infection. *Archives of pathology & laboratory medicine* 2011; **135**(6): 793-6.
Vogt M et al. Enterovirus D68 in the Anterior Horn Cells of a Child with Acute Flaccid Myelitis *NEJM* 2022



AFM Pathophysiology:
EV-D68 Retrograde Axonal Transport





Hixon AM, Clarke P, Tyler KL (2019) "Contemporary circulating EV-D68 strains infect and undergo retrograde axonal transport in spinal motor neurons independent of sialic acid" *J Virology*.

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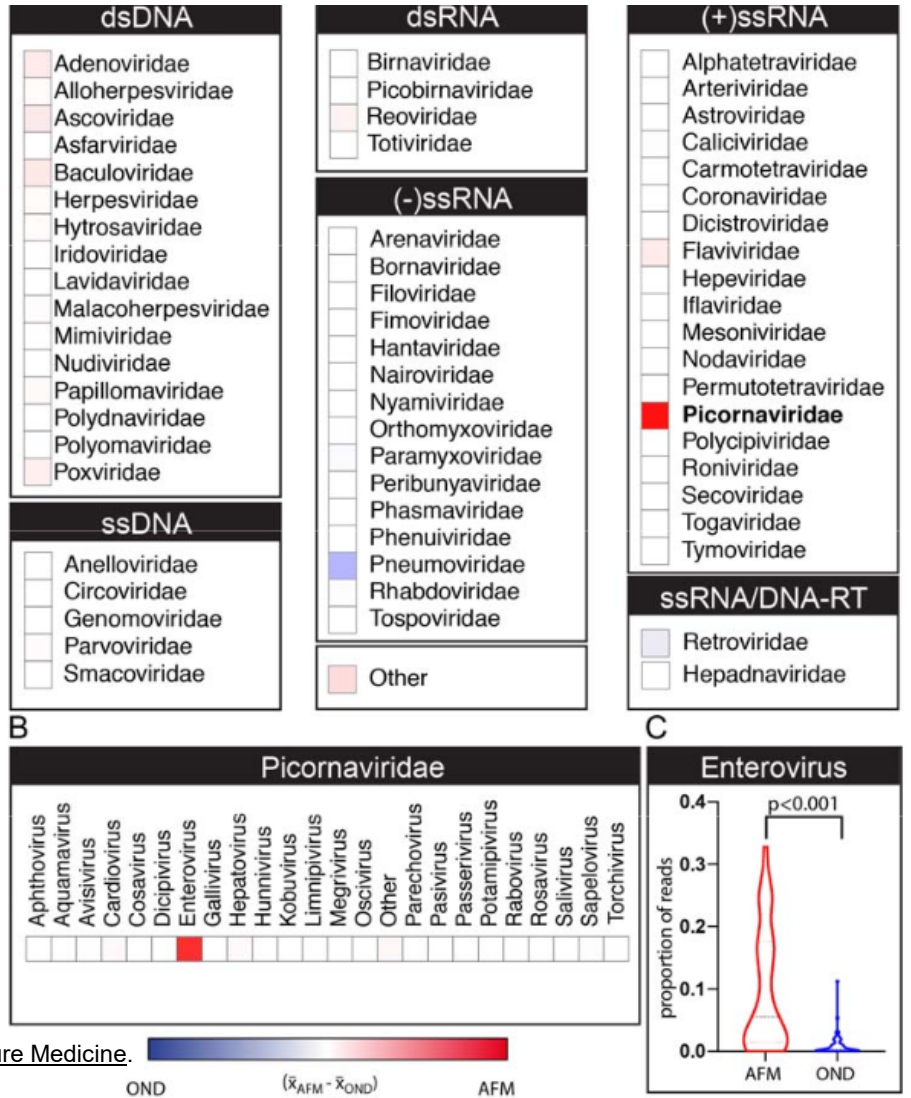
Research Advances in AFM Dx: Panviral Antibody Testing of CSF

- New phage display serologic assays and microarray chip technologies can look for Abs to many viral peptides in CSF
  - High levels of EV Ab detected in CSF of most AFM cases vs. controls (including patients without virus identified in CSF or nonsterile sites)
    - No Abs to other viruses consistently identified

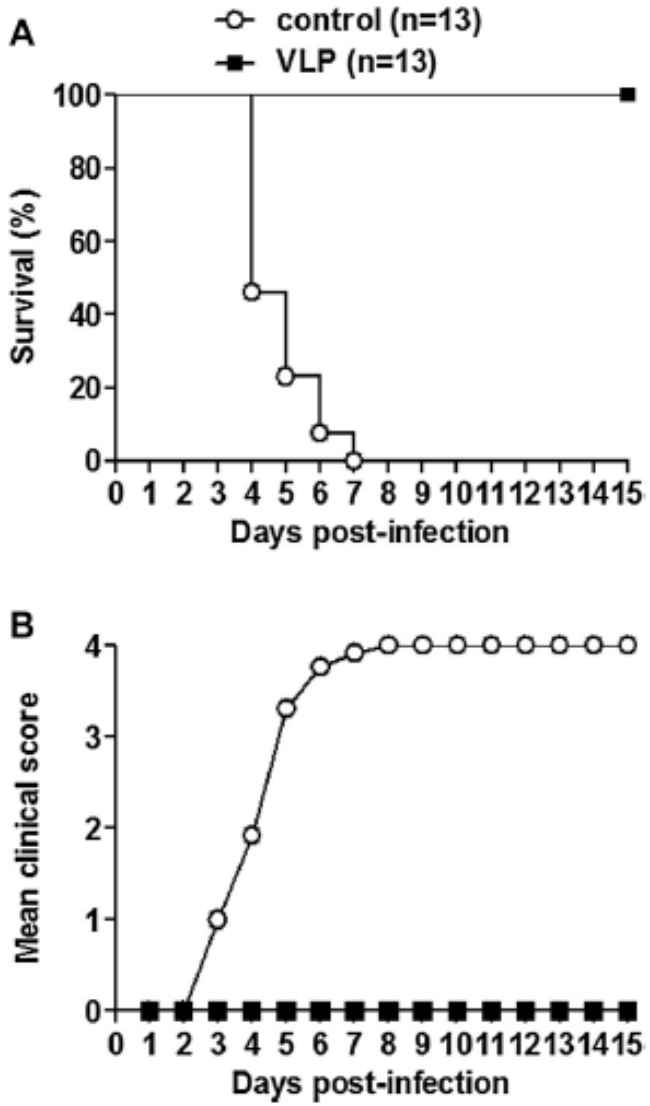
➢Detection of EV Ab in CSF may become clinical diagnostic test for EV AFM, similar to other neuroinvasive viruses (ie. WNV)



Schubert, R et al. (2019) Serological and metagenomic interrogation of cerebrospinal fluid implicates enteroviruses in pediatric acute flaccid myelitis. Nature Medicine.
Mishra, N et al. (2019) Antibodies to Enteroviruses in Cerebrospinal Fluid of Patients with Acute Flaccid Myelitis. MBio

Advances in Preventio
Vaccine Development

- Vaccines can effectively prevent EV disease
  - Poliovirus vaccines, global eradication campaign
  - EV-A71 vaccines licensed in China
    - Efficacy against HFMD, severe disease
- Few EV-D68 candidate vaccines in early pre-clinical stages of development
  - VLP Vaccine (China)
  - NIH Vaccine Research Center
  - Intravacc received NIAID contract to dev'p vax



EV-D68 VLP Vaccine:

Maternal vaccination completely protects neonatal mice from lethal infection

Messacar K, Vogt M, Asturias E, Abzug MJ. Nonpolio Enterovirus Vaccines. *Plotkin's Vaccines* 2021.
Dai W et al. A virus-like particle vaccine confers protection against enterovirus D68 lethal challenge in mice. *Vaccine.* 2018

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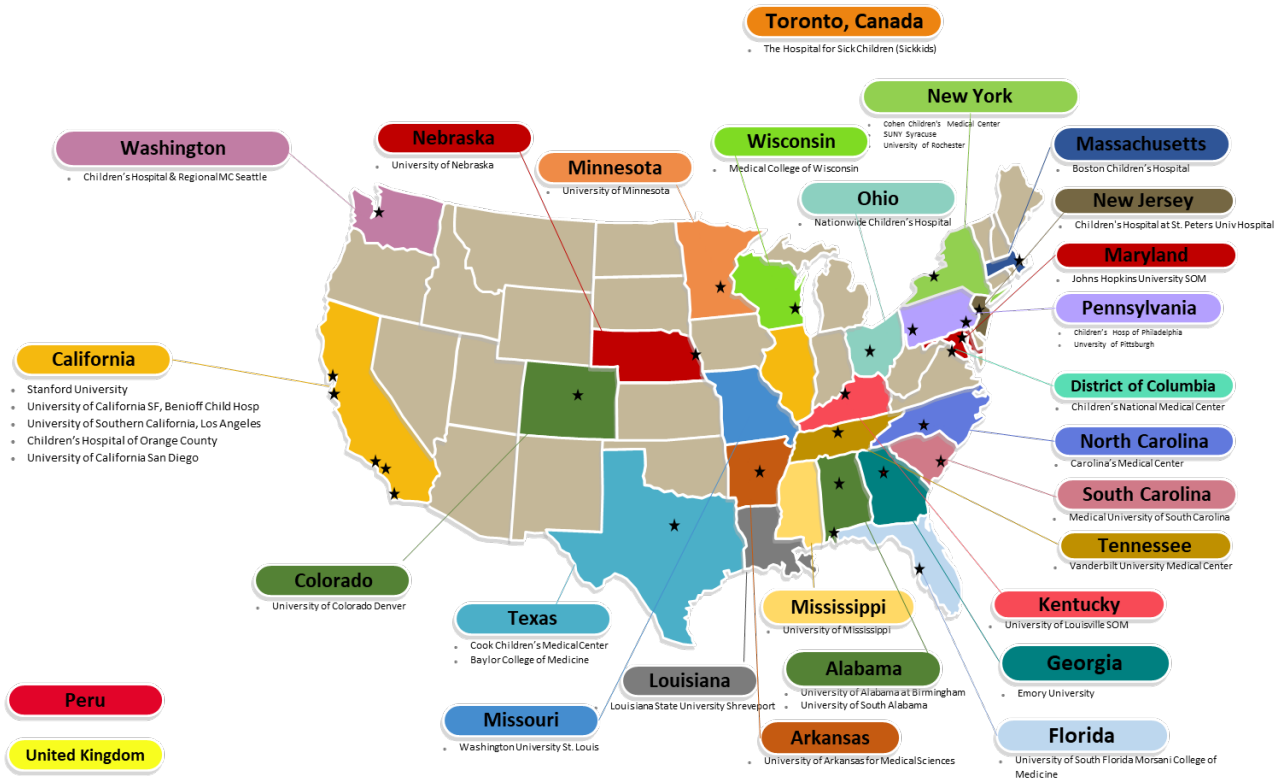
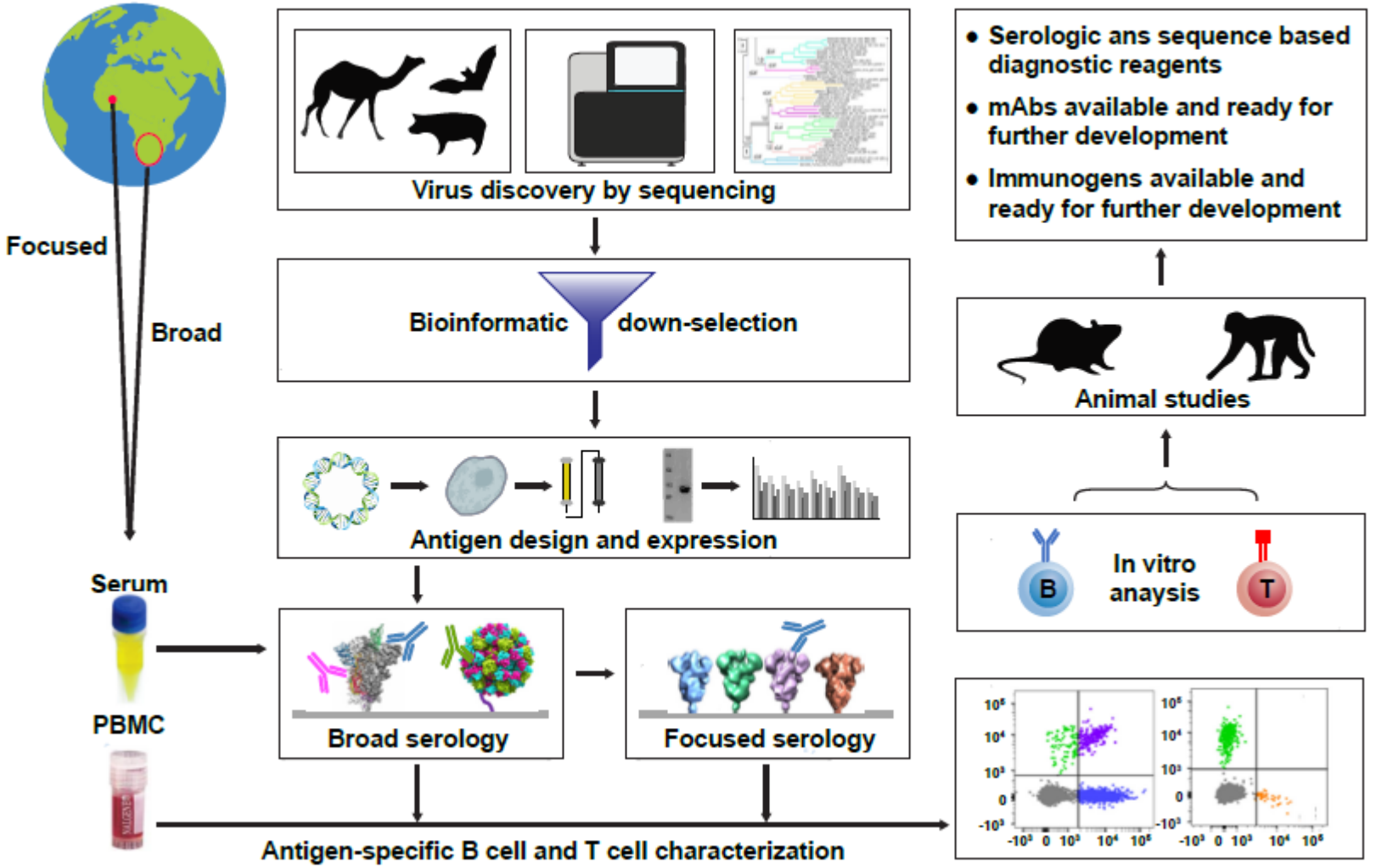
Ongoing Research Efforts: NIAID Multicenter AFM Natural History Study



- 36+ center international (US, Canada, UK, Peru) study of children with suspected AFM and household contacts followed over 1 year to determine natural history and populate NIAID biorepository for AFM research
  - Samples and data accessible through oversight committee

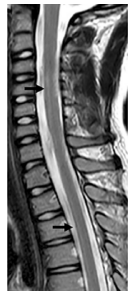
Ongoing Research Efforts:
PREMISE EV-D68 Pilot Study

- **PREMISE:** pathogen-agnostic NIAID pandemic preparedness project to create immunologic biorepository at NIAID Vaccine Research Center
  - Creation of on-the-shelf tools (diagnostics, therapeutics, vaccines) for emerging infectious diseases
- **EV-D68 Pilot:** focused proof-of-principle study using virus with public health importance likely to re-emerge
  - To enroll 500 children <10yo at 4 US sites for collection of pre- and post-EV season blood specimens (serum, plasma, pBMCs)
  - Followed with symptom surveys during EV season to collect respiratory specimen when sx



Nguyen-Tran, H. *et al.* Enterovirus D68: a test case for the use of immunological surveillance to develop tools to mitigate the pandemic potential of emerging pathogens. *Lancet Microbe*, doi:10.1016/S2666-5247(21)00312-8 (2022).

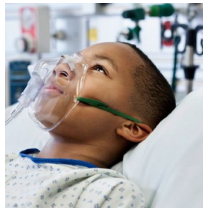
Future Vision:
Comprehensive EV-D68 AFM Surveillance

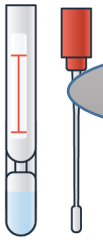


Syndromic Surveillance

AFM

AFM Epidemiology
Etiologic Investigation





Symptomatic Surveillance

Respiratory Disease

EV-D68 Epidemiology
Outbreak Detection
Burden of Disease

Wastewater Surveillance

Asymptomatic Infection

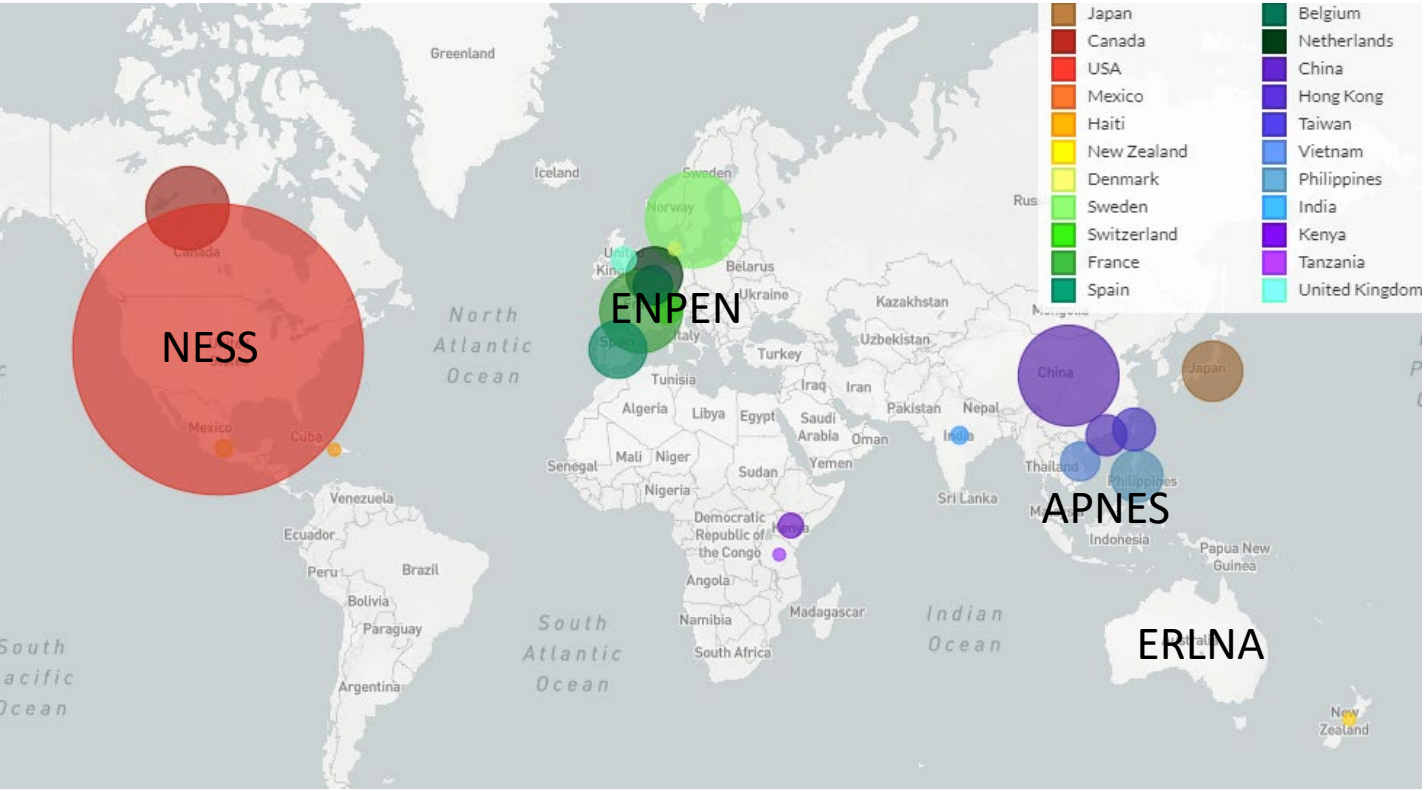
Early Warning System
Phylodynamic Monitoring

Immune Surveillance
Serosurveys

Prior Exposure/ Immunity

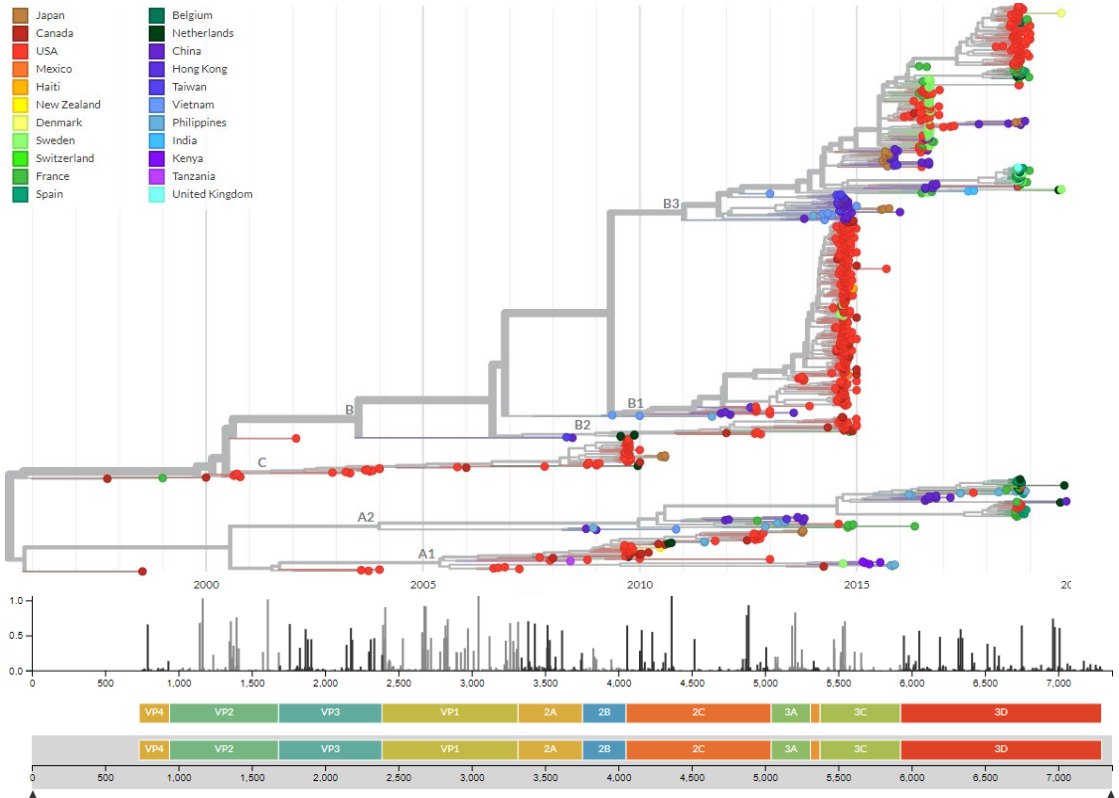
Modeling
Preparedness

Future Vision:
Global EV Surveillance



Real-time Global Sharing of Surveillance Data

- Epidemiological data
- Phylodynamics

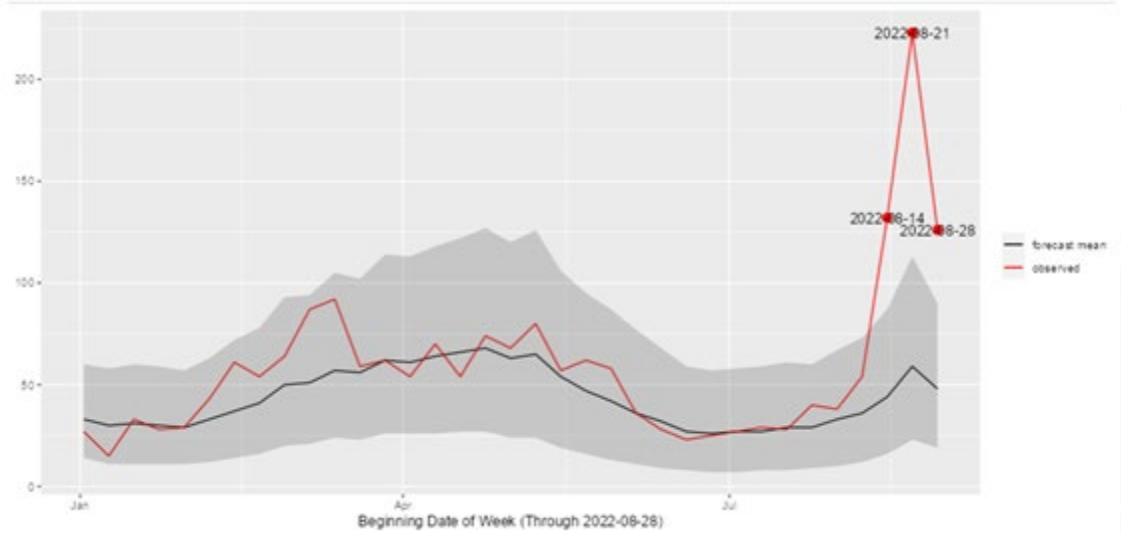


Global Integration of EV Surveillance Networks

- Inclusion of respiratory sampling in polio surveillance

Images modified from <nextstrain.org/enterovirus/d68/genome> Accessed 7/19/22

Prepared for the Present



Severe Respiratory Illnesses Associated with Rhinoviruses and/or Enteroviruses Including EV-D68 – Multistate, 2022

HAN HEALTH ALERT NETWORK

This is an official CDC HEALTH ADVISORY

A MESSAGE FROM
The Leadership Team

To: All Children's Hospital Colorado team members

Dear team members,

Over the past few weeks, emergency departments across our System of Care have seen a significant rise in acute respiratory disease, particularly asth ore than typically see, leading to high numbers of hospital admissions due to respiratory issues. Our monthly census for occupied beds was the highest it has b w leaders working around-the-clock to ensure we have the ability to care for all of these patients.

Our infectious disease and laboratory professionals have identified Enterovirus D-68 (EV-D68) as a contributing factor behind this surge of respiratory disease, and other pediatric hospital systems around the country are seeing similar trends. EV-D68 tends to follow a biennial outbreak pattern and nationwide su were experienced in 2014, 2016 and 2018. Based on prior EV-D68 seasons, we anticipate this current surge may last another six to eight weeks, though much remains unknown given the disrupted circulation of viruses over the past two years of the pandemic.

In addition to causing respiratory disease, EV-D68 can cause limb weakness due to the polio-like neurologic disease, Acute Flaccid Myelitis (AFM). Based on prior EV-D68 waves, we anticipate that we may see a rise in AFM cases in the weeks to come. Given our clinical and research expertise in this area, Children Hospital Colorado is well-equipped and prepared to provide the best care to any child affected. We will be working closely with the Centers for Disease Control and Prevention and Colorado Department of Public Health and Environment to support the public health response.

CBS NEWS NEWS SHOWS LIVE LOCAL Login

HEALTH ›

CDC warns about enterovirus in kids – and the risk of rare paralysis that can follow

BY ALEXANDER TIN
UPDATED ON: SEPTEMBER 12, 2022 / 5:39 PM / CBS NEWS

Challenges for the Future

- **Improved AFM recognition:** early diagnosis, specimen collection, care
  - Limb weakness in setting of febrile illness (esp during EV season): **Suspect AFM**
    - MRI + LP to confirm
      - Collect CSF, blood, NP/OP, rectal/stool specimens
- **Improved surveillance:** AFM and EVs
  - Reporting systems for all suspected AFM cases
  - Active EV surveillance for early warning system, preparedness
- **Improved understanding of pathophysiology**
  - NIH prospective multicenter AFM Natural History Study enrolling in US/UK/Peru
- **Improved treatment and prevention strategies**
  - Therapeutic candidates evaluated in animal and laboratory models
  - Vaccine candidate identification

AFM is currently uncommon, but has serious long-term morbidity

"Watching healthy children become permanently paralyzed virtually overnight by a seemingly random, lightning-strike disease is as heartbreaking today as it was in the polio era. The trajectory of AFM over the past 5 years suggests that the problem is getting worse, and so it is critical that we galvanize our efforts to learn more about, and respond adequately to, this ubiquitous, often crippling, continually reemerging group of viruses."

Morens DM, Folkers GK, Fauci AS. Acute Flaccid Myelitis: Something Old and Something New. MBio. 2019;10(2).

Recognize AFM early

Be alert for onset of acute flaccid limb weakness and consider AFM on your differential diagnosis

Collect specimens & then get MRI

Collect cerebrospinal fluid (CSF), serum, stool, and nasopharyngeal (NP) swab as soon as possible, and handle and store specimens properly

Rapidly report to health department

If the MRI shows a spinal lesion with some gray matter involvement, alert the health department and send specimens and medical records

Diagnosis & medical management

Refer to specialists, monitor for signs of worsening symptoms, hospitalize if indicated, and begin treatment and rehabilitation

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https://www.cdc.gov/vitalsigns/afm/index.html <accessed 7/15/19>

Take Home Points

- **THINK AFM** in any patient with new onset weakness, particularly:
  - Children with **asymmetric, flaccid weakness**
  - Following a **febrile respiratory illness**
  - **Summer-fall** season during enterovirus outbreaks
- **DIAGNOSE AFM** by neurologic exam, neuroimaging, lumbar puncture
  - **Collect early biologic specimens** (CSF, blood, stool, NP/OP) to look for cause
- **MANAGE AFM** with respiratory & neurologic supportive care, rehabilitation
  - **Reach out for help** from neurology and infectious disease consultants
- **REPORT AFM** to your state health department as soon as you suspect it
  - **Submit requested biological specimens** using CDC Job Aid (https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinicians-health-departments.html)

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KEY REFERENCES

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RESOURCES

US CDC Resources for clinicians/public health:
https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinicians-health-departments.html

AFM Working Group Resources for clinicians:
https://acuteflaccidmyelitis.org/

Acute Flaccid Myelitis Association Resources for Parents:
https://www.afmanow.org/

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