Acute Flaccid Myelitis in Children
Daniel R. Taylor, DO,* Sharyu Krishnakumar, MD*
*Department of Pediatrics, Saint Christopher’s Hospital for Children, Philadelphia, PA

An excerpt from *The Atlanta Journal-Constitution* in April 2019 describes a 3-year-old boy from the Atlanta area. "AC scoots around on his bottom in the living room of his Winder home as he plays with a toy train set. When it’s time for school, his mother helps the 3-year-old into a black wheelchair with blue and green bars on the frame and a red Lego robot keychain attached to the headrest." The article goes on to explain that AC has had 4 surgeries and multiple infusions and may require potentially lifelong physical and occupational therapy. "This will never be over for us," his mother agonized in this article. AC was diagnosed earlier in the year as having acute flaccid myelitis (AFM).

Reminiscent of this 2019 article, several children living in small pockets of Brooklyn, New York, in the summer of 1916 awoke and were not able to move their arms and legs. Terrified parents rushed their children to local health centers, where physicians were perplexed by these symptoms, with many physicians having gone through their entire careers without ever seeing a case of what they soon recognized was paralytic poliomyelitis (polio). By December 1916, the polio epidemic had spread from New York City to more than 2 dozen states, spreading to the Midwest. Within 7 months there were 27,000 reported cases of polio, and 6,000 people had died, with thousands more paralyzed or having permanent limb deformities.

Fast forward 70 years to 1987, when doctors in the United States started reporting a few dozen cases of a severe respiratory illness tied to a virus that was first identified as enterovirus 68 (EV-68). Then, in 2008, a 5-year-old boy from New Hampshire contracted a febrile illness with neck pain, paralysis, and eventual death, which was attributed to EV-68. Tragic, but an isolated case, until 2014, when cases of what is now called AFM began to appear. AFM is considered a "poliomyelitis-like" syndrome with similar presentations as polio, which was eradicated in the United States in 1979 through an aggressive vaccine program.

Cases of AFM in the United States have demonstrated a biennial presentation, and most cases present in the summer and early fall. Whereas there were 120 reported cases of AFM in the United States in 2014, there were only 22 in 2015. An increase to 149 cases was noted in 2016, only to drop to 35 cases in 2017. The most recent data for 2018 include more than 220 cases, with this number continuing to rise as more children are reclassified as having AFM. Cases have been reported in 14 countries, including Norway, Canada, France, and Great Britain, but the United States is the epicenter. The alternating-year pattern of this disease continues to be a mystery.

Eighty percent of cases present with typical prodromal symptoms of an upper respiratory tract infection or gastrointestinal illness and fever, a typical presentation for dozens of common childhood illnesses. Yet, a median of 5 days evolves before the presentation of neurologic symptoms such as onset of limb weakness or paralysis, hypotonia, hyporeflexia or areflexia, facial droop or

**AUTHOR DISCLOSURE** Drs Taylor and Krishnakumar have disclosed no financial relationships relevant to this article. This commentary does not contain a discussion of an unapproved/investigative use of a commercial product.


**Enterovirus D68-Associated Acute Flaccid Myelitis Rising to the Clinical and Research Challenges**. Messacar K, Tyler KL. *JAMA*. 2019;321(9):831–832


weakness, ophthalmoplegia affecting the ocular muscles or eyelids, and dysphagia or swallowing dysfunction. Paralysis is rapid (hours to days) and is typically asymmetrical with any combination of limb involvement but with a preference for the upper extremities. The pattern of weakness of AFM points to a lower motor neuron disease process, which is similar to entities such as polio, Guillain-Barre syndrome, amyotrophic lateral sclerosis, and botulism. Cranial nerve dysfunction is seen in approximately 30% of patients.

Although the cause of AFM is still not known, EV-68 is suspected to play a role because this virus has been detected in 47% of respiratory specimens of confirmed cases of AFM when collection has occurred within the first 2 weeks after the onset of symptoms. No other candidate pathogen has been consistently detected in cases of AFM.

The hypothesized pathogenesis of EV-68 playing a role in AFM is a newly enhanced neurotropism of EV-68 with greater potential to infect and destroy neurons. This mechanism has also been demonstrated in laboratory mice infected with recent EV-68 strains.

The average age at presentation of AFM is 4 years; the oldest confirmed case was a 32-year-old man, and the youngest less than 1 year old. Ninety percent of cases occur in children, with most aged 3 to 6 years.

In June 2015 the Council of State and Territorial Epidemiologists approved a standardized definition for AFM used by the Centers for Disease Control and Prevention (CDC) that classifies patients under investigation for AFM as probable or confirmed cases.

The clinical criterion for AFM is an illness with acute onset of flaccid limb weakness. Imaging criterion that supports the diagnosis of AFM is magnetic resonance imaging (MRI) of the spinal cord showing lesions in the gray matter spanning 1 or more vertebral segments. Supportive laboratory results include cerebrospinal fluid pleocytosis (white blood cell count >5/μL [>0.005×10^9/L]).

Confirmed cases, as designated by the CDC, include clinically compatible criteria of AFM along with the classic MRI findings. Probable cases are defined as clinically compatible criteria with a normal MRI but with a cerebrospinal fluid pleocytosis.

To date there is no standard of care for treatment, which has included corticosteroids, antivirals, intravenous immunoglobulin, and exchange transfusions. Hence, early involvement of a neurologist with expertise in AFM is warranted. Children who are affected may need months if not years of physical and occupational therapy and tendon or nerve transfer surgeries to strengthen their weakened muscles and to regain their ability to eat. Recovery, tragically, is often incomplete, with most children having motor deficits and muscular atrophy more than a year after onset of symptoms.

At the present time, the CDC, along with experts in the field, has published interim considerations based on the available evidence (https://www.cdc.gov/acute-flaccid-myelitis/hcp/clinical-management.html). "There is no indication that any specific targeted therapy or intervention should be either preferred or avoided in the treatment of AFM. There are currently no targeted therapies/interventions with enough evidence to endorse or discourage their use for the treatment or management of AFM." The CDC suggests early expedited consultation with neurology and infectious disease experts and reporting of all probable cases to the CDC. Recommendations for testing are published on the CDC website: [https://www.cdc.gov/acute-flaccid-myelitis/diagnosis.html]. The establishment of real-time EV-68 surveillance networks is vital to isolate early outbreaks geographically. There needs to be more outreach to physicians and other health-care providers, including the public, to detect, test, and treat AFM at its earliest onset to attempt to mitigate the worse-case outcomes. Utilization of best practices, networks of care, and advanced technologies in virology and pharmacokinetics are necessary to try to achieve the best outcomes for patients with AFM.

This novel, acute, and, so far, mysterious disorder reminds us once again that nature is constantly evolving along with the pathogens that infect, interact with, and coexist with the human species. This disease is humbling a medical community that is racing to develop improved diagnostic criteria for AFM and to develop standards of care for the hundreds of children who have been affected and will continue to be affected in the future. The medical community must pursue research into the pathogenesis and must study best practices in physical rehabilitation and nerve transfer surgery to maximize outcomes and, if EV-68 is definitively identified as the pathogen, to develop appropriate vaccines. Time is of the essence.

COMMENT: The appearance of a new disease that initially presents with very common symptoms and progresses in a small subset of patients to significant morbidity results in heightened concerns and fears for children, parents, and medical providers alike. This In Brief reminds me of questions that a mentor of mine, Dr Barton Childs, an internationally
renowned geneticist, would always ask us to consider when evaluating patients: “Why this child, why this disease, and why now?” These wise questions seem so poignant when contemplating AFM. A common viral illness (suspected to be an enterovirus but not yet proved) infects many children, yet, fortunately, only a small proportion go on to develop AFM. Of those diagnosed, the morbidity spans wide variability, from weakness in a single limb to paralysis of all extremities. AFM has reminded our medical community of the lessons learned from polio, when education of primary care providers was essential for early recognition and the development of a vaccine resulted in eradication of the disease in the United States. The CDC issued a warning on July 9, 2019, urging providers to consider the diagnosis of AFM as early as possible, to contact local health departments, and to obtain specimens of serum, cerebrospinal fluid, stool, and nasopharyngeal swabs in addition to MRI testing. National and international coordination of efforts is needed to best understand the epidemiology, coordinate multicenter studies to identify best therapies, and develop an animal model for possible vaccine development. In the meantime, the Transverse Myelitis Association has created an around-the-clock support portal for physician consultation when AFM is being considered as the diagnosis. The portal address is https://mvelitis.org/living-with-mvelitis/resources/afm-physician-support-portal/. Although many, many questions remain concerning AFM, the past track record of coordinated medical research provides me with hope that, just as with polio, best practices will be developed and, optimally, prevention through vaccines can be achieved.

– Janet Servint, MD
Associate Editor, In Brief
Acute Flaccid Myelitis in Children
Daniel R. Taylor and Sharyu Krishnakumar
Pediatrics in Review 2019;40;602
DOI: 10.1542/pir.2019-0129

Updated Information & Services
including high resolution figures, can be found at:
http://pedsinreview.aappublications.org/content/40/11/602

Subspecialty Collections
This article, along with others on similar topics, appears in the following collection(s):
Infectious Disease
http://classic.pedsinreview.aappublications.org/cgi/collection/infectious_diseases_sub
Epidemiology
http://classic.pedsinreview.aappublications.org/cgi/collection/epidemiology_sub
Public Health
http://classic.pedsinreview.aappublications.org/cgi/collection/public_health_sub

Permissions & Licensing
Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
https://shop.aap.org/licensing-permissions/

Reprints
Information about ordering reprints can be found online:
http://classic.pedsinreview.aappublications.org/content/reprints
Acute Flaccid Myelitis in Children
Daniel R. Taylor and Sharyu Krishnakumar

Pediatrics in Review 2019;40;602
DOI: 10.1542/pir.2019-0129

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pedsinreview.aappublications.org/content/40/11/602