

Anna Okula, Moderator : Hello, everyone, and welcome to the Centers for Disease Control and Prevention’s webinar, Acute Flaccid Myelitis: What Clinicians Need to Know in 2020.

As the CDC prepares for a possible AFM outbreak in 2020, we want to make sure all clinicians have the information and resources they need to properly recognize AFM symptoms, appropriately manage patients, and report suspected cases.

Before we get started, we wanted to review a few housekeeping items. All participants have been kept on mute to reduce background noise. If you have any questions, please write them in the chat box in the lower right corner of the webinar screen. Please be sure, when submitting a question, you direct it to Webinar Staff by selecting this option on the drop-down menu. We will answer as many questions as we can at the end of the webinar.

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If you continue to experience these or other issues, please e-mail us at AFMwebinar@porternovelli.com, and that e-mail should be in the invite that you received. Finally, this webinar will be recorded and available online on CDC’s AFM website.

And now I’d like to introduce you to today’s first speaker, Dr. Janell Routh.

Dr. Janell Routh: Thanks, Anna. Well, thank you so much, and good afternoon, everyone. We really appreciate you all being here today. It is good to talk about AFM since we may be seeing an increase in cases this fall.

As Anna mentioned, my name is Janell Routh, and I’m a medical officer and lead for the AFM and Domestic Polio Team. I’m joined today by my fellow medical officer, Dr. Sarah Kidd, our lead surveillance officer, Adriana Lopez, and our communications specialist, Dr. Alexandra Hess, who will all be contributing to the webinar this afternoon. Next.

We have no conflicts of interest and have one disclaimer that the presentation will include a brief discussion of off-label treatment options, not approved by the FDA for the treatment of AFM. Next.

I’ll give a brief introduction and then the clinical overview of AFM, including recognition, its initial evaluation and diagnostic studies, and clinical management. After that, I’ll turn the presentation over to Ms. Lopez to provide information on reporting AFM to public health. Next, Dr. Kidd will discuss AFM epidemiology, what we’re thinking about for 2020, and provide a brief summary. And then finally, Dr. Hess will outline our AFM resources for healthcare providers. Next. And next.

So in 2014, as you all probably know by now, CDC was notified of children having sudden onset of limb weakness and gray matter lesions in their spinal cords. If this had been 50 or 60 years ago, we would have assumed that these were due to poliovirus, but poliovirus has been eliminated in the United States since 1979.

Acute Flaccid Myelitis, or AFM, was the term created to describe these patients and distinguish their illness from that caused by poliovirus, although they are clinically similar. More than 90% of our AFM cases reported are in children younger than 18 years of age. And there are a number of viral causes for AFM, including non-polio enteroviruses, flaviviruses, herpes viruses, and adenoviruses. Next.

CDC has conducted national surveillance for AFM since the first cluster was recognized in 2014. This epidemic curve of cases by month of limb weakness onset shows that we've seen increases in AFM every two years, since 2014. Most cases have occurred in late summer through early fall, and 85% of cases do occur between the months of August and November, in those peak years. The curve also shows that confirmed cases appear to be increasing every other year, starting with 120 confirmed in 2014, and reaching a high of 238 in 2018. Next.

AFM has a variety of viral infectious causes, as I mentioned, but it can also have other causes such as neuroinflammatory conditions or spinal vascular disease that share similar clinical and radiographic findings. Not everyone who is infected with these viruses will develop AFM. It's an uncommon outcome of these viral infections, and not everyone who has these other conditions will develop AFM, but all of these can and do produce the clinical and radiographic findings we call AFM. Next.

We believe the mixture of infections and other conditions cause a low-level baseline rate of AFM highlighted here in the red box, which is consistent from year to year. This baseline has likely been the pattern for decades, but clearly something changed in 2014. Next.

And that's the key question: what is causing the biennial peaks that we see in AFM? Next.

One piece of evidence we have comes from our 2014 investigation, which showed a temporal association between one specific enterovirus, D-68, or EVD-68, and AFM cases. In this slide, the large, severe respiratory outbreak of EVD-68 resulted in positive cases, shown by the yellow line and right axis and AFM cases shown by the blue bars, and the left axis. AFM cases peaked shortly after the peak in EVD-68 infections, and Dr. Kidd will talk more about this association in her section. Next.

With that introduction, now, I'll move on to the clinical aspects of AFM, including recognition, diagnosis, and medical management. Next.

In patients who have AFM, almost all describe a preceding febrile illness, one to two weeks before the sudden onset of limb weakness. These symptoms include fever, rhinorrhea, cough, and sometimes vomiting or diarrhea, although those are less common. Many children are still

febrile at the time of presentation. Onset of weakness is rapid, with a progression within hours to a few days. The weakness is described as more proximal than distal and is often asymmetric. On examination, there should be a loss of muscle tone and reflexes. Next.

Cranial nerve abnormalities may be present and include facial or eyelid droop, difficulty swallowing or speaking and a hoarse or weak cry in infants. Weakness may be accompanied by stiff neck, headache, or pain in the affected limbs. And many patients complain of neck, shoulder, or back pain just prior to weakness onset, one of the really striking features of this illness. Uncommonly, patients may complain of numbness or tingling in the arms or legs. Next.

One of the more severe complications of AFM is respiratory failure, which can progress rapidly and require mechanical ventilation. We were told, interestingly, about a child who presented to the Emergency Department with just isolated right leg weakness, and within two hours required emergency intubation and had progressed to quadriparesis.

AFM patients can also have autonomic instability with fluctuating temperatures and blood pressure swings, and those can be life-threatening. So we do emphasize that clinicians should immediately hospitalize patients for monitoring because of this rapid progression. Next.

The differential diagnosis of AFM is broad, and I'm sure this slide resonates with many of you. It's often hard in the initial phases of AFM to determine whether this weakness is due to a spinal lesion, or another condition. The differential includes things like transient synovitis, which can follow viral illness, neuroinflammatory conditions like Guillain-Barré syndrome or transverse myelitis and all the way to stroke or cord compression.

This underscores the point that in the late summer or early fall with preceding symptoms consistent with a viral illness, AFM must be high on the differential diagnosis for acute limb weakness. Careful examination, laboratory evaluation, and imaging of the brain and spine can help guide diagnosis. Next.

So now let's turn to that initial evaluation of a patient with limb weakness. Next.

When taking a medical history, please note any illnesses in the past four weeks, particularly those with symptoms consistent with a viral illness, like respiratory or GI symptoms, and record if fevers were present. Ask about hand, foot and mouth lesions, as this may signify infection with an enterovirus like EV-A71 or coxsackievirus. Next.

A focused and age-appropriate assessment is critical, since young children and parents may actually not see that functional impairment as weakness. We worked with our expert panel of pediatric neurologists to come up with the following list of questions to ask parents during the exams to help with that assessment. And for the sake of time, I'm not going to go through those questions here, but they will be available on our website. Next.

Additional signs and symptoms to recognize, particularly in young children, include difficulty holding up the head, which may indicate weakness of the bulbar muscles, decreased appetite, and difficulty swallowing. Again, headache, neck, shoulder, or back pain that presents just prior to or concurrently with limb weakness, pain in the extremities, increased sleepiness, or inactivity, even though children with AFM are not typically encephalopathic, they can be listless and lethargic.

Interestingly, we recently heard a mother's account where her child's first symptoms weren't a specific arm or leg weakness, but more of a generalized weakness with bulbar signs of difficulty swallowing that progressed to quadriplegia. So it wasn't one limb that actually focused the parent's attention, but that overall decrease in strength and tone.

Finally, please ask about bowel and bladder changes. These are more uncommon in AFM patients, although we do see constipation, but they are useful in differentiating AFM from other neuroinflammatory conditions like transverse myelitis. Next.

A well-documented physical exam is important to help differentiate AFM from other similarly presenting conditions. The neurologic exam should include tone, strength, reflexes, cranial nerves, and sensation if possible. Note that the sensory exam is often normal in AFM patients. We recognize that these may be difficult to do in younger children, but certainly tone and reflexes are very important to that diagnosis. Next.

Additional and key pieces of the exam include an airway assessment and documenting a baseline for respiratory sufficiency to watch over time. Negative inspiratory force may be used if the child is old enough to perform that maneuver. Blood pressure and temperature are pretty standard pieces of information with each admission, but again, they're very useful to mark a baseline to follow through that hospitalization. Next.

And now, to make sure that everyone's awake, we'll do our first knowledge check. Could we please go to the poll? So which of the following can be symptoms of AFM? Please select one of these answers: Sudden onset of arm or leg weakness, facial droop or weakness, difficulty moving eyes or drooping eyelids, difficulty with swallowing or slurred speech, and finally, all of the above.

Okay, and that answer... It looks like everybody is either staying awake, or the question was too easy. The answer is E: all of the above. Most of you got that correct. Next.

So moving on, I'd like now to talk about the key diagnostic studies to obtain with an initial AFM workup. Next.

This is a busy, but important slide. Laboratory testing can help differentiate AFM from other causes of limb weakness. We recommend a lumbar puncture as soon as possible after the onset of limb weakness, and we do recommend routine CSF studies be conducted on that CSF,

along with pathogen-specific testing for bacteria and viruses that may cause meningitis or encephalitis.

Serum should be drawn for pathogen-specific antibodies, as well as for MOG and aquaporin for antibodies, looking for other neuroinflammatory conditions. Stool and rectal swabs are important for testing for entero- and rhinoviruses as well as an NP or an OP swab, testing for the same.

Neuroimaging is important, to look for lesions in the brain and spine, and I'll talk more about those in just a minute. And then, depending on your location, additional pathogen-specific testing may be necessary based on seasonality, other exposures that your patient may have had and geography. Next.

So a few reminders about lab testing. Again, as I mentioned, and I'll emphasize here, these should be done as soon as possible after the onset of limb weakness, ideally, while the child is still in the Emergency Department. We know that samples drawn closest to limb weakness onset give us the best chance of finding a pathogen. We recommend consultation with neurology and ID specialists to help guide testing, particularly for those more nuanced tests, with helping to diagnose neuroinflammatory conditions.

We request that you send CSF, respiratory, serum, and stool specimens to CDC for public health surveillance. We test these specimens for enteroviruses and also for poliovirus. The poliovirus testing is critical to show that the United States remains polio-free, and it is a required component of all acute flaccid limb weakness cases.

And as I just mentioned, ID consults can guide additional pathogen-specific testing based on your location, seasonality, and any other patient exposures. So we do recommend consulting your ID physicians at the hospital. Please contact state and local health departments to coordinate sending specimens to CDC for testing. This may be handled by one of the specialty consults by the primary team or by infection prevention at your hospital.

However, we do want to make sure that all clinicians are aware of reporting, and we'll be talking more about those procedures later in the presentation. Next.

MRI imaging of the brain and spine provide important diagnostic clues for AFM, and these really form the basis of our AFM case surveillance here at CDC. Please order both spine and brain MRI with and without contrast and use the highest Tesla scanner available. Note that images within the first 72 hours of limb weakness may be normal, and we do suggest repeating those if clinically indicated.

Axial and sagittal images are both helpful in identifying lesions, and multiple levels of the cord are often involved with AFM. So if a child can tolerate it, we do recommend imaging the entire spine. For patients with cranial nerve deficits, high cuts of the brainstem and a brain MRI would be useful in that regard.

And then finally, although the hallmark of AFM is really those gray matter-predominant lesions, associated inflammation within the cord may result in white matter involvement also. Next.

So the images on the right — I know that these may be a little bit difficult to see — demonstrate the characteristic spinal cord lesions of AFM. In panels A and B, highlighted by the red arrows, the sagittal and axial images show that gray matter hyperintensity of the thoracic cord. And in B, you can see that characteristic H or butterfly pattern of that gray matter hyperintensity. Panels D and E show the T2 hyperintensity now localized into the anterior horn cells, and that's best seen in image E, highlighted by the white arrow.

We're learning that there is a progression to AFM on MRI. At first, the cord is swollen and edematous, with little localization of the lesion. However, gradually over time that lesion does become localized to the gray matter, and at 10 to 14 days after limb weakness onset, it's really settled into the anterior horn cells. We're still learning how the extent of the lesion correlates with clinical outcome. And we hope that the new AFM natural history study on which CDC is collaborating with the National Institutes of Health will provide information about this question. Next.

So now I'd like to briefly touch on clinical management of AFM. Next.

So the key to clinical management is really hospitalization to monitor and ensure that the patient's airway is secure. Frequent monitoring of respiratory function is important. Knowing that rapid deterioration can occur, and about 25% of AFM cases reported to CDC end up needing ventilatory support.

We recommend consulting, as I mentioned already, with neurology and infectious disease experts to help guide treatment and management decisions. And I did want to let you all know there's a great tool now for clinicians that's available through the Siegel Rare Neuroimmune Association. They have a clinical portal that connects clinicians to AFM experts across the country. You can ask questions about diagnosis or clinical management, and all requests into that portal are returned within 24 hours. So it's a valuable tool, and many of our academic collaborators across the country staff that site.

We also have a clinical considerations document on the CDC AFM website that provides a summary of all treatments that are currently used for AFM and we'll be updating the document this fall. Next.

So treatments commonly used for AFM in the acute phase of illness include IVIG or intravenous immunoglobulin, corticosteroids and plasmapheresis. As you can imagine, given the low incidence of AFM clinical trials to show efficacy are difficult to conduct. Therefore, at this time, there's not enough human evidence to indicate a preference for or an avoidance of their use.

We recommend that the decisions about treatment be made in consultation with experts. Some neurologists do use corticosteroids when evidence of inflammation causing white matter involvements is evidenced on the exam or MRI. But certainly, this must be balanced against the use of immunosuppression in the setting of a viral infection. Again, with that NIH natural history study, we really hope to learn more about treatments across different institutions in the United States.

And then, finally, I did want to mention that, at this time, there's no indication for the use of fluoxetine, antiviral, or other immunosuppressive agents for AFM. Next.

So thanks for your attention. Now, I'd like to turn the presentation over to our lead surveillance officer, Adriana Lopez, to discuss the importance of AFM surveillance and reporting suspected AFM cases to the health department.

Adriana Lopez: Thank you. Next.

Many illnesses, like influenza, for example, have a laboratory test that helps to define the condition. So if we see someone with symptoms, including a cough and fever, and they have a positive laboratory test for influenza virus, we can say with some certainty that they have a case of influenza. Next.

Conducting surveillance for AFM, on the other hand, is challenging, primarily because there is no direct laboratory test for AFM. Although we believe that enteroviruses, and in particular EV-D68, play a role in causing AFM, many cases test negative for these viruses. Therefore, for AFM, we had to create a different system for gathering data and classifying cases, using information like medical records and magnetic resonance images to classify a case of AFM. Next.

In creating a surveillance system, we develop case definitions to ensure that we collect standardized information from year to year, so that we can compare cases across time. These case definitions have changed slightly since surveillance started in 2014, with changes in 2015, 2017, and 2019. Each following the outbreak years, as we have learned something new every year after an outbreak.

However, the definition of a confirmed case has remained consistent and is still the acute onset of flaccid limb weakness and an MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments. Next.

The source of CDC surveillance data for AFM is via health departments from the reporting clinician. Once a clinician recognizes that a patient may have AFM, they should alert the health department to assist in the collection of pertinent medical information, magnetic resonance images, and biological specimens to send to CDC.

CDC works with an expert panel of neurologists to review the medical information and images and provide a case classification. The surveillance case classification is communicated back to the Health Department, and then to the clinician and family. Next.

Public health surveillance for AFM serves a different purpose than making a diagnosis of AFM. I would like to emphasize here that the CDC case classification of a suspected AFM case should never replace or take precedence over the clinical diagnosis. Clinical diagnosis is used for patient-level, individual clinical management decisions, and is time sensitive. A diagnosis is made based on full information, including history, diagnostic testing, and examination. It aims to be as accurate as possible to provide the best care and treatment for the individual.

Public health surveillance, on the other hand, is conducted at the population level. Standardization using case definitions helps to measure disease burden and trends over time. Surveillance can be delayed due to reporting lags and the time it takes for the neurology panel to review images and make a classification. Finally, it has to balance sensitivity, which is wanting to cast a wide net for all possible cases, with specificity, making sure the cases fit a certain mold, so that they can be compared.

We hope that as we advance our understanding of the syndrome and biological markers that predict it, our cases will become more straightforward to classify. Next.

So to summarize, reporting is a critical piece of the AFM surveillance pathway, and it is important for clinicians to report patients meeting the AFM clinical criteria to public health. The AFM clinical criteria for reporting includes acute onset of flaccid limb weakness and an MRI showing a spinal cord lesion in at least some gray matter, regardless of whether laboratory results are still pending.

Reporting of cases should not delay a patient's diagnosis and/or treatment and management plan, and a classification by CDC is not meant to override a clinician's diagnosis of a patient's illness, or their treatment and rehabilitation plan.

Finally, the sharing of information through reporting is critical for gaining a better understanding of AFM and its pathogenesis, to help inform treatment and prevention strategies. More information on reporting can be found on CDC's webpage for clinicians and health departments listed here. Next.

So now we've reached our second knowledge check, if we have the poll up, please. So which is not a way to decide on AFM diagnosis? Please select one. Consult with a neurologist in your institution, consult experts via SRNA's AFM Physician Consult Portal, review information about AFM on the CDC website, wait for CDC to report back on the final case classification, or search for publications about AFM in medical literature.

Okay. And the answer is D: wait for CDC to report back on the final case classification. Next.

So now I'd like to turn it over to Dr. Sarah Kidd, a medical epidemiologist on our team, and she will discuss the epidemiology of AFM.

Dr. Sarah Kidd: Thank you. So I'm going to transition to talking about what we know about the epidemiology of AFM. Next slide, please.

We've already discussed how since 2014, we've seen this biennial pattern with increased AFM cases every other year, in 2014, 2016, and 2018. During previous years, we've seen an increase in cases during August through November, and the peak month is typically during September.

During the in-between years, we see this low number of sporadic cases that we believe represents the baseline rate of AFM in a population due to multiple infectious and noninfectious etiologies. So our question is really what is driving these new peaks every two years, and what changed in 2014 to cause what appears to be a new epidemiology of AFM? Next slide.

And it does look like this really is new since 2014 or shortly before. Even though national surveillance didn't begin until 2014, studies have looked back at MRI and medical records in pediatric hospitals to see if they could find cases that in retrospect were AFM. And the results of those studies have shown that there really were low numbers of sporadic cases before 2014.

And then they also found a similar spike during 2014. So it really does look like this is something new, not something that had been going on for a long time but just wasn't recognized or detected. Next slide.

So since 2018 was our most recent peak year, and we think those cases are most likely to represent this new epidemiology that we're interested in, I'm going to describe the characteristics of the 2018 AFM cases. Next slide.

In 2018, 238 AFM cases were recorded from 42 states, the median age was 5.3 years and the vast majority of cases were in children under 18 years of age. 58% of cases were male, so there's a slight male predominance, and about half identified as white, non-Hispanic, 20% identified as Hispanic, 9% as black, non-Hispanic, and 3% identified as Asian. Next slide.

And to emphasize, again with a map, cases in 2018 came from 42 states, similar dispersed throughout the United States. So we generally don't see clusters or hotspots of cases occurring close together geographically. And this pattern indicates that this is most likely an uncommon complication of a very common infection. Next slide.

In terms of clinical characteristics, 98% were hospitalized, and 54% of all patients were admitted to the intensive care unit. The majority of patients, 87%, had a CSF pleocytosis. And among those patients who did have a pleocytosis, the median white blood cell count was 94

cells per cubic millimeter, so generally a mild to moderate pleocytosis with a lymphocytic predominant.

Limb involvement tends to be asymmetrical and proximal muscle groups are most severely affected, but there is a range of involvement. On initial exam, 37% had one limb affected, but 27% had decreased strength in all four limbs. And there is definitely an upper limb predominance, with 47% having only upper limb involvement, compared to 16% with only lower limb involvement. Next slide.

Almost all cases had some viral prodrome with fever and upper respiratory symptoms being the most common. 80% had a URI prodrome and 77% had a fever during the prodromal period. You can also see that neck or back pain and headache were also common in the days leading up to limb weakness. And if you look at the data displayed on the right, these show you the average interval between the onset of the prodromal symptom and the onset of weakness.

So in general, the quote-unquote classic clinical course for these patients is to have onset of fever and respiratory symptoms first, then a few days later develop headache and neck pain in about the one to two days prior to onset of weakness. These may be important diagnostic clues to make you think of AFM when seeing a child with limb complaints. Next slide.

Unfortunately, diagnostic testing, especially from sterile site specimens like CSF, generally does not identify an organism, and this has made identifying the main viral culprit for AFM more challenging. However, if you look at the results of the nonsterile site specimens like stool and respiratory samples, the yield is a bit higher.

Enteroviruses are the most common viruses detected among AFM patients, and EV-D68 in particular is the most common single virus detected. EV-A71 also contributed to AFM in 2018. There are also a handful of less frequently detected enteroviruses and rhinoviruses, and these include coxsackieviruses, and those are included in the Other EV RV group. Next slide.

Even though we've only rarely been able to directly detect virus in the CSF of AFM patients, two recent studies have provided supporting evidence for the role of enteroviruses in AFM by documenting the presence of viral antibodies in the CSF.

Both of these studies found that enterovirus antibodies were higher in the CSF of AFM patients compared with non-AFM controls. While not quite as conclusive as direct detection of virus itself in a CSF, these results provide some of the best supportive evidence yet for the leading hypothesis that enterovirus infection plays a key role in causing AFM. Next slide.

So this is our final knowledge check. If we could go to the poll. Outbreaks of AFM in the US have been occurring during blank starting in 2014. And select the most appropriate answer. The first option is flu season, every year. Second option is during the holidays. Third option is every winter and spring. And the fourth option is late summer through fall, every other year.

And hopefully, this was relatively easy for everyone. So I think we can just go ahead. Right, so the answer is late summer through fall, every other year. Next slide.

So as I just said, outbreaks of AFM in the United States have been occurring during late summer and early fall every other year. And so this leads us to the obvious question, about what do we expect for AFM in 2020? Certainly based on previous patterns, we had been expecting and preparing for another AFM season this year.

But with the COVID-19 pandemic, we are not sure what to expect. It's very possible that physical distancing measures and other personal practices, such as hand washing and face masks, may decrease transmission of other respiratory diseases, including enteroviruses and EV-D68.

However, there are a lot of unknowns. There may be a spike in AFM cases beginning in August, or there may not be this year, and if there's not an increase, it's possible that the outbreak will just be delayed by a few months, or could even be delayed until next summer. And if it is delayed, will it be the same size or we might even expect a bigger outbreak? So all this goes to say that we prepared for an increase this year, and we will be remaining vigilant for an increase in cases going forward. Next slide.

The good news is that so far, we have not seen an uptick in cases or in case reports so far in 2020. This figure shows the number of suspected AFM cases that are reported to CDC by week of report. The blue line represents the average number of reports we receive per week during the peak years, and you can see that during the peak years we see an increase in reports starting in August. So we believe that this will be our early warning sign that we're starting to see an AFM peak.

Compare this blue line to the yellow line, which represents the average number of reports per week for non-peak years. And you can see that that line fluctuates, but generally remains below five reports per week.

And then this year's data is shown in the red line. So far, we're seeing just that fluctuating baseline, which is consistent with this time of year for both previous peak and previous non-peak years. So, so far, so good, but we remain on alert for an increase in these case reports going forward. Next slide.

So to summarize what we've covered so far, go on to the next slide, please.

There are a variety of healthcare professionals and specialties involved in addressing AFM. We rely on all these clinicians for recognizing, diagnosing, reporting, and, of course, managing AFM during both the acute illness and rehabilitation phase to optimize recovery and long-term outcomes. Next slide.

Here are some of the most important points that we'd like you and healthcare providers to take away with them today. AFM patients can deteriorate quickly, and weakness can rapidly progress and lead to respiratory failure. In terms of recognition, most patients have a preceding febrile illness about a week before developing limb weakness, most commonly a respiratory illness. Patients also complain frequently of neck or back pain and headache in the days leading up to limb weakness. So these should be clues that make you think of AFM in a child who presents complaining of weakness or decreased use of a limb.

If you are thinking of AFM or any neurologic cause of weakness, perform and document a thorough neurologic exam including strength, reflexes and tone. These patients should be hospitalized immediately for monitoring of vital signs and respiratory function, and in terms of specimen collection, yield is higher early on during the course of disease, and identification of a virus does have some implications for prognosis.

Testing also helps rule out other treatable causes of these symptoms. So do obtain respiratory, blood, CSF and stool specimens in these patients as soon as possible. And order an MRI, with and without contrast, of the full spine and brain to help establish the diagnosis.

Finally, we do recommend consulting with neurology and infectious disease experts early on to guide treatment and clinical management decisions. The next slide.

We have a number of provider resources where clinicians can get more information about AFM. So I'd like to hand it over to Alex Hess, who should talk more about these. Thank you.

Alexandra Hess: Thank you, Sarah. Next, please.

So I would like to cover the resources that we have now created for clinicians about AFM. The number one resource, of course, is our CDC's AFM website. You see the link, [cdc.gov/acute-flaccid-myelitis](https://www.cdc.gov/acute-flaccid-myelitis). You can also just use search engines and Google CDC AFM and it should come up.

I'm showing a list of resources there, one of which is a clinician job aid, which includes help with specimen collection and reporting to public health.

Then we have new webpages, insights for clinical presentation and initial evaluation and diagnostic studies. That was covered today by Dr. Routh, so you can go back there, you can go online after this presentation, and look at those questions that she was mentioning that can help with the initial evaluation of patients.

We have a new slide set also, with some of the slides that you've seen today, that you can use if you want to present about AFM to your colleagues.

There's an FAQ webpage, with questions from clinicians and from health departments, to help answer any additional questions, and also up-to-date surveillance data that are being updated

now once a month. And we will increase this frequency if we see an increase in cases to a once-a-week update.

In addition to this AFM website, we released a Vital Signs Report last year in 2019, with the first summary of the AFM cases from the 2018 outbreak, and you can go look at that data. It includes an MMW Report and fact sheet for clinicians, and a webpage. And we will be releasing a new Vital Signs Report this year in August, on August fourth, that will dig down a little bit deeper into the 2018 cases and review, in depth, all the clinical characteristics and some of the things that Dr. Kidd was talking about today. Next.

In addition to resources for clinicians, we have also resources for parents. We have new webpages for parents, and also a fact sheet and a symptom poster. This month, we will be releasing webpages that will contain stories from families affected by AFM, in recognition of AFM Awareness Month. July has been established as AFM Awareness Month, and this is the first year of recognizing that.

In addition, we had an AFM parent information session on June 25th, to support parents with children affected by AFM. More of these will be planned and advertised as they become scheduled. Then we have an e-mail box for parents and public inquiries, AFMquestions@cdc.gov, where parents and the public can reach us with questions.

And we're working with parent advocates such as the Siegel Rare Neuroimmune Association, and the Acute Flaccid Myelitis Association, to support parents. Next.

In addition, to prepare for this possible increase in cases this year, we have prepared all of these continuing education opportunities to reach more clinicians about AFM. And clinicians can claim several different types of Continuing Education credits. Please claim your CE credits for this webinar. After it concludes, you can go to the webinar's webpage, and we offer several different kinds of continuing education. There's more information about how to obtain it on the webpage.

In addition, on July 21st, we will have another opportunity to reach more clinicians and the public about AFM, and this will be through Public Health Grand Rounds dedicated to Acute Flaccid Myelitis. This will be on July 21st at one PM Eastern Time. The topic is Acute Flaccid Myelitis: Answering Questions Through National Collaborations. And you can go to the webpage, cdc.gov/grand-rounds. This event will also offer credits, and there will be four speakers, including Dr. Routh, Dr. Messacar from Colorado, Dr. Erbeling from NIH, who will speak about some of the research NIH is supporting, and we will also have a parent guest, Rachel Scott, who will talk about the parents' perspective and parent efforts to raise awareness about AFM. Next.

And finally, clinicians can use several different ways to ask questions about AFM for reporting. Clinicians should contact health departments, and we have a list of state and local health departments on our AFM website. If you don't know who your contact is for AFM,

you can go to the website and find a contact.

Then, as Dr. Routh mentioned earlier, clinicians can consult on a suspected case of AFM through the SRNA portal for clinicians. And we also have this link on the website, on the CDC website, as well as the Siegel Rare Neuroimmune Association's website.

And finally, for urgent inquiries, please contact CDC's Emergency Operations Center, and for nonurgent inquiries, clinicians can contact AFMinfo@cdc.gov, and this will go directly to our medical team, who can answer any questions. Next.

With that, here are just some final resources, our website, the contact for clinicians in the portal. And I will hand it back over to Anna.

Anna Okula, Moderator: As a reminder, if you have a question, be sure to submit it in the chat box at the corner of your screen. Please direct your question to Webinar Staff by selecting this in the drop-down menu. So our first question this afternoon: Do we anticipate any impact of COVID-19 on AFM?

Dr. Janell Routh: Anna, thanks so much. I think Dr. Kidd certainly outlined what we think may take place. It's hard to speculate, but with all of the social distancing that has been going on, mask wearing, increased hand hygiene, we do wonder if this will have an impact on viral circulation in general. So lots of different respiratory viruses, including EV-D68 and enteroviruses.

If that's the case, we may not see as big of a spike this year in AFM cases. That spike could never happen, it could be delayed, as Dr. Kidd mentioned, or it may be smaller.

One thing that we need to consider — and we were just talking about this today as a team — is if we don't see an increase in cases this year, does that mean there will be more susceptible people next year and will we see a larger outbreak? So again, it's hard to speculate, but we certainly are prepared in case we do.

The team has been working very hard, as Alex highlighted with all of our resources, to raise awareness this summer, and we certainly are poised to roll into outbreak response, should we see that increase in cases.

Anna Okula, Moderator: Great. Thank you. Our next question: What is CDC doing to make certain that emergency rooms across the nation are abreast and knowledgeable about AFM? As we know, time is of the essence, and it starts at the ER department. How do we help keep AFM top of mind, especially during these peak seasons?

Dr. Janell Routh: So exactly what we're doing right now, raising awareness. One key piece of information we have learned from a deep dive into our 2018 cases is where children present

for that initial visit. That will be forthcoming. That information will be forthcoming in our Vital Signs release in August.

But we do know that we have to target our frontline providers, those emergency room physicians, clinicians, and urgent care clinicians as well. So we have been really working to raise awareness among those groups.

We've been giving webinars specifically to urgent care clinicians. We gave one last month, and next week we will be presenting to the Urgent Care Association. So really, we are trying to target our efforts to those professional organizations and raise awareness.

As well, I think our messaging to the public has been stronger this year around AFM. We want parents to realize that limb weakness is a medical emergency and that they should not be afraid to seek medical care.

I know there have been a lot of parents who have not been going to general pediatrician visits. We know rates of vaccination have been decreasing, because people, I think, are worried about catching COVID, either in a medical clinic or in an emergency room.

But our emphasis this year is really that limb weakness is a medical emergency. Do not be afraid to call your physician and seek care immediately.

Anna Okula, Moderator: Thank you. Our next question: Is it possible for AFM symptoms, specifically limb weaknesses, to resolve completely and then return months or even a year later? Or once symptoms are identified, are they constantly presenting and progressing?

Dr. Janell Routh: That's an interesting question. I will say that I don't know of cases where we've seen that sort of intermittent remitting and relapsing symptomatology. For the most part, when limb weakness occurs in a child, it's because they have those spinal cord lesions, which are attacking the motor neurons in the spine, and that does lead to limb weakness. That manifests almost immediately.

So we can talk a little bit more about patient outcomes, but I would say that we've not seen to date somebody who has had those limb weakness symptoms completely resolve and then re-present.

Anna Okula, Moderator: Great, thank you. Our next question: What is the mechanism of injury to the cord: direct virus or autoimmune?

Dr. Janell Routh: Yes, the question about pathogenesis is one that is critical, and I think it's something that we, as well as many of our collaborators across the country, are very interested in learning more about. I think there's a big debate in the medical community about how these viruses affect the cord.

Just exactly as the questioner asked, is this direct viral invasion of those motor neurons similar to what we have seen in the past with poliovirus or is this more of a post-infectious process, where we have autoantibodies that target the nervous system, similar to what we see with transverse myelitis?

Dr. Kidd, I know that you have been thinking a lot about this idea of pathogenesis. I don't know if you have anything to add.

Dr. Sarah Kidd: I think I would just add that I think most people believe at this point that there is at least a direct viral damage. And that a large part of the neuronal injury is due to direct virus damage. The question is, is there autoimmune or other immune damage as well, and if so, how much? So I think that's a part. But there's probably at least some viral injury.

Dr. Janell Routh: And I will say that one thing the CDC lab is busy looking at right now are chemokine and cytokine levels and increases in AFM patients compared to non-AFM controls, and looking to see whether the immune system is activated, and what kind of immune system release is going on at the time of acute injury. So hopefully, we will have some data about that question very soon.

Anna Okula, Moderator: Thank you. So the next question: What are the long-term effects of AFM?

Dr. Janell Routh: Yes, so this is something that CDC, again, is very interested in looking at. We know anecdotally from speaking with other collaborators across the country and from some publications of case series that the outcomes of AFM are a broad spectrum. Some children do recover fully, and others have long-term deficits, long-term paralysis. We know there are many children that remain in wheelchairs, on ventilators.

Interestingly, we have heard from many parents that children tend to continue to improve over time. So we really do emphasize that ongoing rehabilitation, both physical and occupational rehabilitation, can really help children, and they can continue to make progress even years after that initial injury.

Ms. Lopez, I might turn it over to you to talk a little bit about what we are doing on our team to investigate outcomes of AFM.

Adriana Lopez: Sure. Thanks. So as part of our surveillance in 2018, we started asking outcome questions. So for the 2018 cases, moving forward, we are asking about their outcomes at three different time points: 60 days, six months, and 12 months, post their initial onset of limb weakness. So we've collected data for a lot of the 2018 cases. We're in the process of reviewing that and analyzing that.

And we're also going to be going back to our 2014 to 2017 cases, and collecting some information, one time point, to find out their outcomes, so we can get a better understanding of what's happened with these cases over time.

Dr. Janell Routh: And I will also point out, I know I mentioned a couple of times during my presentation, there is a new AFM natural history study that is being conducted through the National Institutes of Health. CDC is also collaborating on that effort, and this is going to be enrolling suspected patients with AFM. So patients with limb weakness, and following them through their hospitalization, rehabilitation up to 12 months after their initial weakness onset.

And so we're also hoping that that really in-depth look at the natural history of these children will also help us understand a little bit better about initial presentation, and then the resulting outcomes.

Anna Okula, Moderator: Great. Thank you. So I'm going to ask our final question for this afternoon: Regarding reporting, should only patients with limb weakness and MRI gray matter changes be the only children reported?

Dr. Janell Routh: Ms. Lopez, I'll let you take that.

Adriana Lopez: So that's our criteria for reporting, because what we've found is that definitely acute onset of flaccid limb weakness is an important characteristic among patients with AFM. And the spinal cord findings are another key feature. So those are the two criteria that we are asking.

We started out very broad initially. As I mentioned, our case definition has changed over time, just because we've learned new things after each peak year. So what we've learned is we started out with just acute onset of flaccid limb weakness, and that was very broad.

We weren't getting a lot of reports, because I think clinicians were already thinking, this is something else. So they weren't reporting everything that had acute onset of flaccid limb weakness. So looking at those data, we narrowed it down a little bit to try and be a little more specific about these cases of AFM. So that's why we're asking for the limb weakness and the MRI findings as well. And it doesn't have to be predominant gray matter. It's just any gray matter on the MRI is what we're asking for.

Anna Okula, Moderator: Great, Well, thank you so much. There are a handful of questions that we didn't get to today, but we will collect those and respond directly after today's session. Janell, I'll turn it back over to you to bring us home.

Dr. Janell Routh: Well, I just will say, as I said in the beginning, we thank you so much for your attention. AFM is and remains a priority at CDC. Our team has worked very hard this summer to raise awareness, so we appreciate you tuning in and listening to the presentation. And please, as Anna mentioned, any questions that you may have, we're here to answer them. So

reach out to us through our mailbox or through Porter Novelli and we'll make sure to answer all of those questions. Thank you all so much for your time.

Anna Okula, Moderator: Thank you to all of you. So this concludes our webinar. Like Dr. Routh said, if you think of a question, please feel free to e-mail it to us. We will be posting this recording, the transcript, as well as a PDF of today's presentation to the website, so keep an eye out for that. And remember, you can get the continuing education for today's webinar on the website. So thank you all for joining. We'll talk to you soon.

Dr. Janell Routh: Goodbye, everyone.