The Role of CDC and Public Health in AFM Surveillance

Part II

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Rebecca Whitney: [00:00:00] Welcome to the SRNA Ask the Expert podcast series, a special edition in collaboration with Centers for Disease Control and Prevention, Division of Viral Diseases, or CDC. This podcast is entitled "CDC and the Role of Public Health in Acute Flaccid Myelitis, or AFM, Part Two. My name is Rebecca Whitney, Associate Director of Pediatric Programs with Siegel Rare Neuroimmune Association, or SRNA.

[00:00:30] SRNA is a nonprofit focused on support, education, and research of rare neuroimmune disorders. You can learn more about us on our website at wearesrna.org. I spoke once again with Dr. Benjamin Greenberg of the University of Texas Southwestern Medical Center, Dr. Janell Routh of CDC, and Emily Spence Davizon of the Colorado Department of Public Health to discuss even more about AFM in regards to outbreaks, communications, diagnostic criteria, and how we're preparing for a potential outbreak.

[00:01:08] You can learn more about our individual speakers in our previous podcast, as well as at our website.

[00:01:14] Welcome and thank you all for joining me again today. In our last podcast, we really talked about the role of CDC and public health in the process of reporting and surveillance. And today I'm hoping to clarify a bit more about what we mean by outbreaks and surveillance and being prepared for a potential outbreak. Personal protections from COVID-19 helps avert an anticipated spike in 2020 of EV-D68, an enterovirus strain responsible for an every other year spike of AFM.

[00:01:48] Do we expect that this strain will return, and a potential spike of AFM will happen in 2021 as our behaviors and precautions change and as we open communities and start to emerge from the pandemic? Dr. Janell, would you like to start us off with that?

Dr. Janell Routh: [00:02:07] Rebecca, it's a great question. I think this is the question on everybody's mind this year. What will we see in 2021? You know, in years past, we've seen this every other year spike in AFM cases usually occurring in that even your pattern, 2014, '16, and '18. So now that we have skipped 2020, will we maintain that same pattern and see an outbreak in 2022? Or, because we did not see one last year, might we see one this year?

[00:02:40] I think it's hard to predict. In, in the words of Dr. Mark Pallansch, one of my mentors here at CDC, I would say that we can't predict, but we can prepare. And I would just like to say to everybody listening that AFM remains an agency priority here at CDC. You know, everybody knows that CDC is very focused on COVID and the COVID response, but AFM still maintains that high priority status. So, we are busy preparing raising awareness this summer, and certainly if we do see an increase in cases, our team is prepared to respond.

Rebecca Whitney: [00:03:20] Excellent. Thank you. And talking about that particular enterovirus strain and those spikes, is that the only cause of acute flaccid myelitis? Are there other potential causes or is it really that we focus on that one that is the cause for those spikes? Dr. Greenberg, would you like to?

Dr. Ben Greenberg: [00:03:44] Yeah, so I think it's first and foremost important to note, there are multiple potential causes for the clinical syndrome acute flaccid myelitis. So, at its core, and this is what, if we revisit in history, all the conversations that we had over the last eight years or so, this was the cause of a lot of problems at the beginning of trying to organize our, our efforts around the various stakeholders for tracking this.

[00:04:12] Because in one hand, acute flaccid myelitis is a syndrome. It's not one etiology positive. It's not just enterovirus-D68. There are multiple potential causes. But if you ask the question, "what is the most common cause of this syndrome on even years between the months of July and November?", overwhelmingly the most common cause is enterovirus-D68. And so, it depends on how you ask the question. I think this caused a lot of angst and confusion for a lot of folks, because unlike the days of poliomyelitis where the virus was essentially synonymous with the condition by overwhelming numbers, but even then, there were probably other viruses causing paralysis, we just weren't identifying them.

[00:05:05] That is not the same scenario for enterovirus-D68 and AFM. And so really what we've come to understand is the surveillance, the awareness, and the testing of individuals who show up with the syndrome of acute flaccid myelitis is critically important so that we can identify the multiple potential causes.

[00:05:28] But why does EV-D68 get so much attention, is because if we look at the last six to 10 years as a single entity, it's probably responsible for the overwhelming majority of acute flaccid myelitis cases in kids in the United States, and probably the United States and Europe. So, from an epidemiology perspective and a public health perspective, there are very good reasons we're focusing on this virus, because it has caused so much harm to so many people.

Rebecca Whitney: [00:05:58] Excellent. Thank you for that clarification. And what determines an outbreak? How will we know if we're seeing an outbreak in 2021, and how is that information communicated to states, to local communities, to academia medicine, and also to families?

Dr. Janell Routh: [00:06:19] One thing I did want to say is the very practical nature of what we do here at CDC, which is look for cases. So, over the past five years, we really tried to build a strong and robust surveillance system for AFM to help us detect that first increase in cases so that we can make the public, our clinicians, and our public health departments, more aware of what's happening.

[00:06:43] But we also recognize that just looking for an increase in cases already puts us a bit behind the eight ball. And I think, what we need to do is to be looking for an increase in the viruses, that viral circulation that actually leads to cases of acute flaccid myelitis. And so that is one thing we have been working on at CDC. We don't have a nationwide active system for enterovirus surveillance, but we do have sentinel site surveillance.

[00:07:12] So, particular sites across the country that are able to tell us in real time what they are seeing on the ground in terms of viral circulation. And we are actively talking to those partners and looking for the first signs of an increase in enteroviruses, which then might indicate to us: be prepared, that could be followed by an increase in AFM.

[00:07:37] Once that happens, again, there is a robust network across the country to make sure that everybody is informed of what's happening. And Emily, I thought maybe from a state perspective, you might talk to us a little bit about that system.

Emily Spence Davizon: [00:07:51] Yeah. Let me talk about that real quick. And then I'd like to also just briefly mention what Colorado is doing, because we have a couple of different surveillance sort of tripwires or triggers set up if you will. So, both CDC and the state of Colorado utilize something called a health alert network messaging system, which we refer to as HANMS.

[00:08:10] Those are basically like really dense memos that we can send to providers. And we can also target it a little bit to like emergency departments, clinical laboratories, hospital infection preventionists, and those are just these bulletin-type memos that go out with like a really quick sort of urgent need to know, like, we want you to act on this kind of information.

[00:08:34] So we have our own network in Colorado. Sometimes we write our own HANM messages. Sometimes CDC writes them and then shares them. Literally they can just kind of press a button and folks have access to those through a secure messaging portal that state health departments have with CDC. So, it, the transmission of those messages between agencies can happen pretty much in real time.

[00:08:58] First they're screened to see if they maybe have an enterovirus in them. And then we'll, they will test a subset of those to look for enterovirus-D68. When we're talking about if we may or may not start that screening earlier just because things are a little topsy-turvy, there is a traditional enterovirus season, but, as Janell and Dr. Greenberg said, we don't, nobody can really predict, we can just prepare.

[00:09:22] Another thing that we track pretty closely is we work with a really talented modeler who gets data from outpatient and emergency department asthma visits, because we saw a market increase in those in 2014, because enterovirus-D68 was causing a lot of respiratory illness when it was circulating widely in Colorado.

[00:09:41] And there was just a huge spike beyond what the model would have predicted for that time of year. It was very out of season. So, we, weekly, we run the model. By we, I mean the really smart modeler by the name of Kevin Berg. He runs that model weekly. So that, that is, we hope, an early warning system as well for community-wide or increasing circulation of enterovirus-D68.

[00:10:03] And, as Janell mentioned, you know, some partners for wider enterovirus testing, we also just started a CDC-supported project that's going to look more widely at enterovirus and neurologic illness. So, it's a pretty broad umbrella, and we're going to be sending lots of specimens. If we have patients that are enrolled in this, we're going to be sending all of those specimens to CDC for sequencing and, and enteroviral typing.

[00:10:30] So those are the things we're working on. And also, we just, what we hear from providers is another little alarm bell for us to say, is this, is this an outbreak? So, we have some very astute providers at Colorado who will say, you know, gosh, I have never seen this many kids with, you know, hand-foot-and-mouth disease.

[00:10:47] Is this a sign that enterovirus-A71 might be circulating? Or again, those increases in respiratory illness in kids that's a little out of season, right? It doesn't really happen during cold and flu season. So, as Janell said, we're trying to prepare, and we've got a few systems in place so that we're not just relying on one system alone.

Rebecca Whitney: [00:11:04] Great. Thank you so much. And if there is an outbreak, what can, or what will CDC and other partners do in that situation? Can it be stopped? COVID is obviously on everyone's mind. Can it be stopped similar to stopping the spread of COVID-19? Can we do the same with, with AFM or rather with enteroviruses?

Dr. Janell Routh: [00:11:29] One thing is that enteroviruses are, are all around us. And, you know, it certainly appears that the COVID mitigation strategies that we used last year and this year, the masking, the social distancing, the isolation, and quarantine measures did help stop certainly the spread of COVID and other viruses.

[00:11:50] We saw very little influenza cases last year, as well as very little enterovirus circulation. But I think we would all also agree that the commitment to those measures is difficult to sustain. Enteroviruses generally cause a very mild and limited illness. And usually, you know, we all know that A FM is an uncommon outcome of, of this very commonly circulating virus that, as Emily was referring to, you know, causes an upper respiratory infection and sometimes asthma-like symptoms. By the time we see AFM, that enterovirus that has caused it has likely already been circulating in the community.

[00:12:37] And so, it's very difficult then to I think adopt those kinds of very strict measures that we have seen over the past year. What we can really do when we start to see an increase in AFM cases is just raise awareness. I do think that we know getting the children identified as having an AFM, getting them hospitalized and into care rapidly is incredibly important.

[00:13:06] We know that the disease can progress over a 24-to-48-hour, 72-hour period. And so, making sure that they're hospitalized and receiving care is, is incredibly important. And we also know that I think early rehabilitation, even in that acute phase, can really help children with AFM. And so, that is one thing that CDC is very much poised to do really, once we see that increase in cases, start to raise awareness amongst the various communities, including the general public and parents. We want to give them the information so that they can know what to do if they see signs and symptoms in their children.

Rebecca Whitney: [00:13:44] Great. Thank you. And Dr. Greenberg, would you like to add to that as well?

Dr. Ben Greenberg: [00:13:49] Yeah, I think Janell's right. I think we definitely want to raise awareness as we're seeing, if we, if we do see spikes in cases. And from the treatment perspective, I think there's two things... Well, from the patient management perspective, there's two things we want to do. So, so one is making sure our clinicians are aware of the processes for reporting and testing patients who present with acute flaccid myelitis.

[00:14:15] We, there is no way for us to approach research development, understanding, better treatments, unless we get an accurate representation of what's going on in the community. Data and information matters. And clinicians and families are the gatekeepers to us getting access to that data and information.

[00:14:36] So we need to partner with families, we need to partner with clinicians, and not just raise awareness, but understanding of how to share that data with public health authorities and surrounding individuals. But the second is on raising awareness about treatment options. This is not a 'once you're affected, there's nothing you can do' situation. There, while there have not been randomized controlled trials of interventions, and we are working on empirical data sets, which are our lowest class of data, there is a wealth of experience in the world of some things that we think should be done early and often and then after the acute setting to try and improve the outcomes in kids who are affected.

[00:15:17] And so, getting connected with families who have been through this before, centers who have treated these patients before is critically important for individuals who are going through this. And then finally, there are a wealth of research initiatives going on nationwide. Some at individual centers, some coordinated by the CDC, some coordinated by the NIH, and some where all three of those stakeholders are coming together.

[00:15:44] And for families who are willing to give the incredible gift of sharing their information, their data, and their experience in a structured format with researchers across the country, that gift goes a long way for us being better at this in the future. And so, hopefully, our wish is that no family has to go through this ever again. Our expectation, unfortunately, is that this will happen again at some point, whether it's 2021 or 2022, this will not be the last time we see an acute flaccid myelitis patient.

[00:16:16] And so, anything we can do collectively as a community to get better prepared for the next go around is an incredible opportunity that we don't want to miss. And so, being aware, being on the lookout, reporting the data from a public health perspective, looking for opportunities to treat, looking for opportunities to rehab, and then sharing experiences in a scientifically sound, structured way are a lot of things we can do in the midst of what is a frightening and terrible medical event.

Rebecca Whitney: [00:16:48] Excellent. Thank you. So, how does increasing awareness and conducting surveillance of AFM now or during an outbreak help CDC, medical providers such as yourself, Dr. Greenberg, and families learn and understand. You talked about research and sharing data through research. Can you talk a little bit more about what that means for future cases, future outbreaks, future interventions? Is it possible that we can change outcomes in AFM with this information? Dr. Greenberg, if you want to elaborate a little bit more on that?

Dr. Ben Greenberg: [00:17:28] Yeah. I, I think there's really two meaningful outcomes for sharing dat-, for having a good structure for collecting the data and then having families willing to share their data. And I think we've learned these lessons during the incredible times of a global pandemic with a virus.

[00:17:51] So, viruses in general are really tough infectious agents to treat. And, and they're tough for a variety of reasons. The first is the outcome of a viral infection can be dramatically different depending on the person who gets infected and the version of the virus they get infected with, this notion of mutations and changes.

[00:18:18] And it's important to note that whatever version of a virus a person starts off with may not be the version of the virus they end with as the virus mutates within the body constantly during the infection. And so, one of the things that makes viruses difficult is their incredible mutation rates, their ability to have incredibly different outcomes for each individual.

[00:18:39] So, the overwhelming majority of people who get infected with viruses in general have little to any symptoms or mild symptoms. There are, we are constantly getting infected with viruses that we are completely unaware of. And it's only in the right circumstances that you get a symptomatic infection.

[00:18:57] And it's only under very specific circumstances that you get a life-threatening or health-threatening infection. And we've seen this with the COVID pandemic, and we've seen this with the numbers. And so, from a viral infection perspective, treating acutely somebody infected with a virus is actually really difficult.

[00:19:16] We've got lots of antibiotics. We do not have lots of antivirals. And in fact, if you look at the antivirals we have, they really work for chronic viral infections. We really don't have antivirals for acute viral infections. So, in our armamentarium of therapies in the acute setting, we are always working on other ways to support a person's health and limit damage from a virus because we don't have a direct way of clearing the virus.

[00:19:45] We need a person's immune system to do that. And so, what we found, what happened, and I've never borne witness to this before in my medical career, was during a pandemic with literally millions of people getting infected all at once was as a, a group, the medical establishment was able to move through clinical trials at a speed that I have never seen before and get to answers - this worked, or this didn't or what was to be expected.

[00:20:17] Certain therapies worked at certain stages of an illness in certain individuals. And we could carve out groups where this therapy might make sense where it wouldn't make sense for another. For rarer viral infections, where the morbidity is rarer, and enterovirus-D68 -associated acute flaccid myelitis is a great example. It's not one out of a hundred individuals having severe life-threatening infections like with COVID-19; it's one in a hundred thousand to one in a million range where we see these really bad outcomes.

[00:20:53] Doing those types of clinical trials are, I don't want to say it's impossible, but it's going to be really hard to do prospective randomized controlled trials for a rare outcome such as this, I think is going to be incredibly difficult.

[00:21:08] So what are we left with? We're left with tracking the patients' experiences in real time for the empiric therapies we do in as systematic way as possible. And so, what we need and what, with our partners in public health at the local and state level and the CDC, have come up with, our networks are sharing that data so we can start to get a sense of, is there anything I'm doing that might be harmful to a patient? Or are my outcomes worse than what we're seeing elsewhere or better, or the same? But just as, if not more important than that, the data is going to be really important for us to make decisions about future vaccine development.

[00:21:46] And the most effective therapies we have had in medical history has been around vaccines. Because to prevent an illness is the ultimate cure. To eradicate an illness from the planet is incredible. We don't worry about smallpox anymore and that's the only human viral infection that's been eradicated.

[00:22:14] There's a second cow virus that's been eradicated. But those are the only two. We, we're two down, several thousand to go. But as we work on deciding should a vaccine be developed, what are the risk-benefit profiles of our vaccine, and what should we target with the vaccine? The data that's collected goes a long way at informing us as a nation and our public health colleagues on what are those interventions that make the most sense, and should we be pursuing a vaccine on a broad scale? And so, the data, those decisions cannot be made without reliable public health data. And there, there's no way we will get there without that data being shared.

Dr. Janell Routh: [00:22:58] I would just add to what Ben so eloquently said. I really feel like the difference between where we were in 2018 and where we are today are those networks and partnerships that have been built over the previous three years. We've always been in communication with our state and local health departments, and we instigated AFM surveillance starting in 2015 after that 2014 increase in cases in Colorado.

[00:23:25] But I think what really happened in 2018 was a coming together of not just public health, but public health together with our academic clinicians, public health with our parent partners, and forming those strong relationships. So, I really do feel like moving into this enterovirus season this summer, we're strongly positioned to help each other learn more should we see an increase in cases.

Rebecca Whitney: [00:23:53] Great. Thank you. And recently, a new ICD 10 code was adopted specifically for acute flaccid myelitis. Can you give us a few more details about how that will work to inform and get us to a better understanding of acute flaccid myelitis and what that means for our families?

Dr. Janell Routh: [00:24:15] This, I think, was a really incredible partnership between clinicians, parents, and public health. And I do want to give credit where credit is deserved. Robin Roberts really spearheaded this effort and, and saw it through to fruition.

[00:24:30] So yes, beginning in October of this year, this new ICD 10 code will be available for acute flaccid myelitis. It really will be used by health care professionals like Dr. Greenberg to better support disease

surveillance, to help with our understanding of the clinical management of patients, and then also associated costs, illness costs of AFM. Certainly, from a public health perspective, this new code will provide us with a better understanding of surveillance.

[00:25:04] Like how, how many cases of AFM are we seeing across the country based on these ICD 10 codes? It will be sort of a compliment to the active surveillance system that is already happening right now. This case-based surveillance where we get reports from health departments like Emily up to CDC.

[00:25:26] This will also be another way that we can track the number of cases of AFM across the country. And again, have a better understanding of prevalence and incidence of this illness. That, in turn will lead, I think, to the generation of public health dollars and policy to support vaccine development and other treatment modalities.

Rebecca Whitney: [00:25:48] Thank you. Dr. Greenberg, how about your take on that ICD 10?

Dr. Ben Greenberg: [00:25:53] Yeah. It's a critically important step, and it's an interesting piece of the puzzle, just to put it in perspective. So, some people may be paying attention to the news these days around some of the arguments happening around census data.

[00:26:06] So every 10 years, the United States is supposed to count all of us who live in the United States, and it gets used to decide apportionment of congressional districts and, and voting as well as a whole host of other things related to the finances of the country, and every 10 years we update it. And there are arguments over the validity of the data, the accuracy of the data.

[00:26:28] And there's a lot at stake with that data. A lot of decisions are going to be made based on how accurate accounts you got in terms of how many people live in this zip code. It's the same thing for medical conditions, getting accurate data just to count. Not, not understanding the why's, the where's, the outcomes; just a 'how many?' is important.

[00:26:49] And it's, it's incredible to think about the scale, the size and scale of what we're talking about. So, there are between, depending on the year, 8- to 900 million outpatient visits to hospitals in the United States per year. So, so if we round up to 900 million, so almost a billion outpatient visits per year, spread out over 365 days, you get a sense of, there are millions of visits every single day happening throughout the U.S. health-, healthcare system every day of the year.

[00:27:24] So, to get everyone to stop all of a sudden and say, well, how many acute flaccid myelitis patients did you have? We're, we're never going to be able to penetrate into the trenches to get every practitioner, every person checking in a patient for a lab or an x-ray, to fill out a form about a patient's experience. The, the shorthand we use, and to be clear, it's mainly used for billing purposes because these codes get used by third party payers to decide around what treatments are reasonable and what should be paid for. But those billing codes are a great shorthand for us with our modelers that Emily was talking about, our statisticians, to go through and get a sense about the number: how many people in the U.S. did a clinician think may have had acute flaccid myelitis?

[00:28:14] It doesn't delve into diagnostic criteria. It doesn't delve into what testing did they get. The code will be used inappropriately. Some people will get the code and they don't have acute flaccid myelitis. Some people with acute flaccid myelitis may not get the code associated with them. So, it's a very imperfect tool, but still an extremely valuable one to just get a sense.

[00:28:35] Because if all of a sudden Janell says to me, 'well, Ben, we know of a hundred new AFM diagnoses this past year in the United States,' and I say, 'Janell, the ICD 10 code was used a thousand times,' somebody is off. It, it might be Janelle's numbers. It might be the billing numbers. And, and part of what it tells us is where do we have work to do? Do we need to educate people about the diagnostic criteria because they're using it inappropriately?

[00:29:05] Or do we need to educate people about reporting because they're not telling their state and local health departments about their cases. So, getting that diagnostic code, and again, I give credit to the families and the individuals who not only worked hard to get it done, but recognize that something as inelegant, as unsexy, as a diagnostic code has far-reaching implications for a lot of things that happen down the streams. So, I look forward to being able to, being able to use a specific diagnostic code in my clinic, knowing that we're contributing to the overall dataset for the nation.

Rebecca Whitney: [00:29:43] Great. Thank you so much for that excellent explanation of how that's used and in what we'll, we'll gain from that in the future.

[00:29:51] And talking a bit more about surveillance and diagnostic criteria. I know we covered it a little bit in the last one as well. And Emily had given an excellent analogy of a cookie cutter for that surveillance criteria. And I know that recently there was diagnostic criteria published for acute flaccid myelitis.

[00:30:14] And I'd just like to reiterate the difference again, between the two, if even briefly, as far as who uses the surveillance criteria and what is, and who uses the diagnostic criteria. Dr. Greenberg, if you want to start us off on that one again?

Dr. Ben Greenberg: [00:30:34] There's really three different levels of classification that we need to talk about. So, and, and again, this is my framework for it. I'm very curious to hear both Emily and Janell's revision of this. So, but the three buckets I think about. So, there are formal public health defined surveillance criterias... Again, it's like the census.

[00:30:59] So, let's say I have a house in Dallas, and I work in Oklahoma and have an apartment there that I live in Monday through Friday. Where should the census count me in terms of what is my home? Is it Oklahoma or is it Dallas? So, they, they came up with rules and they said, well, if you do this, this, this, this, and this, we're going to call your home Dallas versus Oklahoma.

[00:31:28] And it's kind of an artificial set of rules, but we have to count me in one place or the other in order for the census to make sense. So, we, we, sometimes there, there are, you know, the babies that have to be divided by Solomon. A decision has to be made on where we're going to draw the line, and the surveillance rules are exactly that.

[00:31:48] So, there are criterias there to get a count. They're not perfect. I can make an argument why my home should be Oklahoma instead of Dallas, and it's a very valid argument. But we have to make tough decisions, and those criteria are set up to make those tough decisions so we have a reliable, consistent data set that can be used for analytic purposes.

[00:32:08] Now that's different than some criteria we sometimes set for research studies at an institutional level. So, let's say I'm enrolling into a clinical trial. I may use surveillance criteria or tweak it for the purposes of research. So, I may enroll patients into a study who didn't meet the surveillance criteria, but I still put in that same bucket.

[00:32:31] So there might be different criteria used for a research study. And then, finally, there's me as the clinician making a diagnosis. And that is really, it's taking the criteria that exists, the data I'm aware of, my experiences as a clinician, and saying, does this individual fit mostly into the AFM criteria or not?

[00:32:53] And we've, this has been something that we've had to address over and over again in our clinic, where there are individuals who are in a gray area who didn't get counted in an official statistic, but I thought met enough of the criteria for acute flaccid myelitis to classify that in that way. And it caused a lot of stress and anxiety for us, for families, because they felt like they were getting two different diagnoses.

[00:33:19] And as Janell likes to remind folks, surveillance criteria is not a diagnosis. It is a tool for public health. Just like I may make a diagnosis in someone, and they don't fit criteria, I'm not going to argue to keep changing the criteria every month, because there's always going to be somebody who falls slightly outside that scope.

[00:33:40] And the criteria is there for very specific reasons in order for us to get accurate counts over time. So, there are differences. The, the definitions are different based on the situation. And the criteria get revisited as we get smarter. So, the criteria we use now are different than what we started off with.

[00:34:02] They've been tweaked. And one of the things we, I think, have sorted out very well over these seven years working with the CDC, working with our public health officials, working with families, working with the Siegel Rare Neuroimmune Association and clinicians is to sit around a table together and really sort out, are we designing criteria that is going to exclude too many people who we, in our gut, think shouldn't be counted?

[00:34:29] Or, just as concerning, could we be including somebody in the AFM category who actually had a totally different disease? Both of those errors require vigilance on our part. And it's something we revisit I'd say almost at an annual basis at this point with the Task Force meetings, where there is time dedicated to discussing is this operationally working or not?

Rebecca Whitney: [00:34:53] Thank you very much. I was just going to ask if, you know, speaking about enterovirus and outbreaks and EV-D68, does the surveillance criteria or, and/or the diagnostic criteria require a positive enterovirus infection? How is that pertinent to, to either of those? Is there an infection at all that is required in either of them to arrive at an AFM classification or diagnosis?

Dr. Janell Routh: [00:35:30] Well, I'll speak for the surveillance piece and let Ben talk about diagnosis, because again, you know, diagnosis gets back to the art of medicine. And I think you heard Ben talk very well about all of the pieces of information that go into making that diagnosis, where surveillance criteria are, are fixed and, and fairly straightforward.

[00:35:51] AFM is unique though, because most diseases that CDC conducts surveillance for do have a laboratory test associated with them, but AFM does not. So, an infection, a positive laboratory test for enterovirus, is not required to fit the CDC case classification for a confirmed case of AFM. We based that classification on two things. One, clinical information, so the presence of acute flaccid weakness in one or more limbs, and then the radiographic information that we receive from the MRI of the spine.

[00:36:27] So, those are the two criteria that we look at to make that case classification. Very different than the myriad of, of bits of information that are collected at the bedside with the physician actually viewing the patient in order to make a diagnosis. And I'll, I'll just say two more things. One is that as you heard Ben talk about all of the pieces that go into that diagnosis, you understand that it needs to be done rapidly and efficiently in order to get the care and treatment that patient needs.

[00:37:03] Through our last podcast, we sort of walked through the different steps to get to the case classification process. Ben sends patient information to Emily at the state health department, who then sends the information to CDC. We then send it to our panel of expert neurologists that we have to read those MRIs of the spine and make a case classification. That takes time. It can take upwards of a couple of weeks to a month, and certainly we don't want people waiting for that case classification in order to make any diagnostic decisions about the patients.

[00:37:39] So I think it was a good question because it really does highlight the key differences between diagnosis and surveillance, certainly the information that goes into both and the time it takes for each to happen.

Rebecca Whitney: [00:37:55] Great. Thank you. And Dr. Greenberg on the diagnostic side.

Dr. Ben Greenberg: [00:38:01] Yeah, on the, on the diagnostics side, I mean, I think it is... We get better at this as we go, not just in terms of more awareness, so a broader net being cast, but also in terms of what we should be looking for. So, I, when we started with acute flaccid myelitis and, and Janell thinking back, I don't know if we met for the first time in 2014 or if it was the year later, but somewhere in that 2014 to '16 range, when we were all getting together, we weren't talking about anti-MOG antibody associated disease presenting with an acute flaccid myelitis picture with kids with gray matter lesions and flaccid paresis.

[00:38:44] And that, that was not a topic of conversation at those meetings. And it was only once we started recognizing that, hey, there are these kids who meet a diagnostic criteria for AFM, where we could find an alternate cause, a noninfectious cause. And so, we know that the syndrome acute flaccid myelitis can be diagnosed in a variety of children.

[00:39:06] So we don't require enterovirus-D68 or a specific etiology to diagnose a child with acute flaccid myelitis. And this is where semantics become important but also dangerous. What confused us for so long is polio, poliomyelitis was synonymous with the viral infection. So, when we got rid of the virus and the rates of acute flaccid paralysis, acute flaccid myelitis just dropped off the face of the radar for the United States, we stopped watching.

[00:39:45] And so, the first patients who I saw with acute flaccid myelitis, I didn't even have a lexicon to describe what I was seeing. I called them atypical transverse myelitis. It was, I was a moron. I did-, I literally didn't have the, the vocabulary to truly articulate what was going on because we had always assumed it was poliovirus that, that does this.

[00:40:09] And I remember when first talking with Carol Glaser from the California State Health Department, who described some of the first cases in 2012 out of California. And we had had some cases and I called a colleague of mine who had, had trained in India and I described our cases and he said, Ben, this sounds like polio.

[00:40:29] I said, well, I've never seen polio before. That's when little pieces of this started to come together. So, I have very much resisted the notion of enterovirus-D68 syndrome is acute flaccid myelitis. I've embraced acute flaccid myelitis can be caused by a variety of different things. And in each patient, we need to work in an efficient manner to sort out what the cause is, both for individual patient reasons and public health reasons.

[00:41:00] But recognize that if we test appropriately and track appropriately, we can pick up on these outbreaks that can have a single cause and then target our public health resources around investing in treatments or prevention or vaccines, or what have you.

Dr. Janell Routh: [00:41:15] And Rebecca, I'll just say one more thing, which is that I think that is almost purposely why we're keeping our surveillance for AFM broad and not homing in on a specific virus. We, you know, there was a perfect example in 2018 where we saw 11 cases of AFM, again in Colorado, that were caused by a different enterovirus, enterovirus-A71.

[00:41:41] And so, realizing that vaccine development and the development of treatments for AFM can take time and resources. We don't want to pin all of our hopes on one virus and then end up having to pivot at the last minute. So again, to Ben's point, there are multiple causes of AFM, and I think continuing to look broadly for all of those causes serves us all well.

Emily Spence Davizon: [00:42:06] If it's okay, just wanted to tag on to two things that Dr. Greenberg said and then one thing that Janell mentioned. So, you know, you had talked about the upcoming ICD 10 code, and we just discussed that, you know, there is further surveillance, and it sounds like the clinical, you know, there's no requirement for any sort of positive enterovirus test.

[00:42:26] And that goes back to what we talked about previously is that's one of the fundamental reasons why surveillance for acute flaccid myelitis is rather different from most other surveillance that we do, because it is, is not and cannot be laboratory based for a variety of reasons that both Janell and Ben have talked about.

[00:42:44] And I think the introduction of the new ICD 10 code means that I kind of have to change my stump speech about why AFM surveillance is challenging because I would be like, look, it's a syndrome, have to rely on provider reports, there's no lab test, and there's literally not an ICD 10 code. So that's just to say that, like, I'm, I'm rather thrilled that that is changing because the absence of the ICD 10 code and the absence of like case-based, lab-based case finding, you know, takes away some of our surveillance tools.

[00:43:18] So getting, getting another surveillance tool to do a little bit more big data stuff is, is really exciting. And, you know, Janell mentioned that diagnosis should never depend on and should never wait for the surveillance case classification, and that can take some time. I do want to sort of toot CDC's horn here a little bit, because that process used to be slower.

[00:43:39] That process used to be more winding and curvy than it is now. And at one point, I got to participate a little bit in sort of looking on when sort of like a step-by-step look at all of the different procedures that happened in the case classification took place. And they sort of did like a type of like a lean analysis, would that be accurate Janell?

[00:44:02] But really looked at like wait-limiting steps, and it's much smoother. And I was just like at my keyboard like, 'yes, this is better'. So, thank you. Like, they, CDC has been responsive. CDC, in my experience, you know, has looked for, you know, what, what would be helpful here. And it's also, in my experience, helpful for clinicians too, because it makes it a little bit clearer, a little bit faster to have that feedback loop to share with patients and families.

Rebecca Whitney: [00:44:30] Yes. Thank you so much. And that's something that I'm continuing to hear and learn as we've had these different outbreaks, is that the communication, the flow of it between the various partners in, in public health, in supporting families, amongst families is what is, is key to understanding and making sure that everyone's aware of getting those acute treatments as quickly as possible.

[00:44:58] One quick question I do want to ask is if, if a family suspects acute flaccid myelitis, or a physician who hasn't probably seen a case before suspect's AFM and they look to CDC for answers about next steps. Is there anything, Janell, that you'd like them to know? What should they, they do to make sure that they are

seeking getting a diagnosis as quickly, as accurately as possible so that we can hopefully improve outcomes for that child?

Dr. Janell Routh: [00:45:31] Rebecca, thanks. So, you know, certainly our, the information that CDC has available on our website for AFM has increased substantially over the past seven years. And I would definitely say over even the past just two years, there is now a new page just for parents where they can go and find lots of different resources, including just basic information about AFM.

[00:45:58] Research opportunities that they can look at and potentially enroll in to, again, participate in some of that data sharing that we need so desperately across the country, in order to understand AFM better. We also have - and ben can probably talk about this because he was instrumental in standing this up, as is SRNA - the new physician portal, the clinical portal where physicians, clinicians can go and request a consult, an expert consult on their patient in order to speak with an expert and talk about that diagnosis.

[00:46:37] So, many different resources available on the CDC website now that I would definitely encourage parents and clinicians to take a look at. I think, you know, we always talk about parents really being advocates for their child. And the more informed they are about the condition, the more they can speak to their clinician about, one, diagnosis and, and making sure that their child gets the care they need.

[00:47:07] And then secondly, reporting that case into public health in order to provide that information forward so we can all learn. I think I mentioned on the last podcast, but I'll say again: we do learn from every single case of AFM, regardless of whether it turns out to be confirmed or probable, or we consider it not to be a case. We learn from every single patient, every single child that's reported.

Rebecca Whitney: [00:47:33] Great. Thank you so much. And then, as we talk about being prepared for a potential outbreak, or even just to be prepared for that one family who may be experiencing a possible acute flaccid myelitis diagnosis, what, what are we doing to be prepared?

[00:47:52] You spoke a lot about the resources and information that is available on CDC's website. Dr. Greenberg, how about from the, the clinical side, from the, the perspective of, of your clinic that sees a lot of these cases. Do you have preparedness plans in place for when they come potentially to you this summer?

Dr. Ben Greenberg: [00:48:17] Yeah. So, we've been partnering with the Texas Department, State Department of Health and Human Services around raising awareness, doing education around the 20 to 25 pediatric hospitals who are in our region, not just in Texas, but in neighboring states, trying to partner with physicians on the front lines, emergency room physicians, hospitalists to recognize signs and symptoms and get neurology involved early and shorten the clock between a patient presenting and being recognized, worked up, reported, and treated appropriately.

[00:48:53] One of the things we're doing as we raise awareness is always revisiting our data to decide as patients pop up, what are the tools in our armamentarium to use in the acute treatment? And what we're also doing is trying to listen very carefully to the experiences of our existing families who have been dealing with the long-term sequelae of this illness and trying to look for patterns of what worked or didn't work for them.

[00:49:22] And one of the patterns we've seen not in a scientifically gathered way, but in an empirical way is the impact of early intensive rehabilitation therapy for these kids and a very close eye after- in the acute setting and after the acute setting. And we've been working hard with families to try and keep them engaged in the rehabilitation mission.

[00:49:45] And I have to say, you know, every year that goes by, I keep waiting for some of our kids who are four or five, six, seven years out to plateau. And I have to say, for all the families who are just really pushing hard, and it is multiple full-time jobs to do this, to, to balance school and work and life, and just being a kid on top of the requirements of therapy.

[00:50:12] I mean, it's, it is a mammoth task. But we keep seeing it pay off. We see, keep seeing our kids acquire functions and, and improve functions over time. It's slow. It's slower than any of us would want, but it's there. And so, one of the things we're reminding families and clinicians, even in the acute setting and gearing up for it is, we want to see physical therapists at the bedside in the hospital, not just when we go to rehab.

[00:50:38] We want to be aggressive with the rehabilitation we do. And then we're constantly looking for medical therapies that can limit the amount of damage that would occur to the spinal cord. And so, we're gearing up. I'd love to see no outbreak this year, but if there is one, I think at our Center, we'll be ready both to report what we see, record what we see, and hopefully help the patients we see get better.

Rebecca Whitney: [00:51:03] Great. Thank you so much. And I know we work closely with, with families as SRNA as well, and being able to connect them with other families and with clinicians, and clinicians to clinicians and supporting that AFM consult and support portal to make sure that physicians who are looking for that consult can obtain one.

[00:51:28] But also for families who aren't sure of next steps and may need some information of what they're looking for or what questions to ask of their provider. Emily, I know you spoke a little bit about it earlier, too, about some of your preparedness plans and your work with, with the, the local hospital.

[00:51:50] Anything else that you'd like everyone to be aware of as far as what you're doing to be prepared for that potential outbreak or that individual family?

Emily Spence Davizon: [00:51:59] Absolutely. Thank you. There is one other thing, which I don't know that I mentioned on the last podcast, but it's related to that provider database that I talked about that we can use to send out 'Dear Provider' letters to.

[00:52:12] And, you know, we can segment it by pediatricians. We can segment it by family nurse practitioners, all that kind of stuff. So, we used that database late last fall and sort of late last winter to send out about 6- or 7,000 surveys actually to pediatricians, family medicine doctors, family nurse practitioners, those kinds of folks.

[00:52:35] So, more primary care providers. And ask them a whole bunch of questions about, have you heard of AFM? Do you know it's reportable? Do you know how to report it? What information would you like about AFM and how would you like to get that information? And so, we're finishing up an analysis of those survey results that we hope to use to guide both our outreach and public health.

[00:52:55] And we're also actively sharing those survey results and findings with our clinical partners, because we also have a relationship with our clinical partners to do more like doctor to doctor, nurse to nurse type of outreach. So, we're trying to get better at what we've done since 2014 and really, really target that.

[00:53:16] And I actually also have a meeting on my calendar for next week to start talking about talking about what is our communication plan and really preparing some of that messaging beforehand in the hope that we never have to use it. And also, just make sure that that messaging is very tightly coordinated between public health and between our clinical partners.

[00:53:35] And when you were kind of asking about what, what about, how does this preparedness impact families and things like that? And the one thing that occurs to me is that when we increase awareness among parents and families, you know, like Janell and Ben mentioned, it, it means that they may get to care sooner, it means that they can start rehab sooner.

[00:53:55] It may, you know, influence outcomes. And the other thing that, to me, that awareness can provide for parents and families is the opportunity to connect to social support. Janell flew out to Colorado back in 2018, I think, so that we could do some really in-depth in-person interviews, which was something that, you know, we hadn't had a chance to do before because of lack of resources, lack of time, et cetera.

[00:54:19] And one of the things that was really striking to me in those interviews was the difference that social support made in addition to sort of that more medical, physical support. But having other people know what you were going through, having other people to have casual conversations with about, 'Hey, my kid met this milestone,' or 'Hey, I'm struggling with this, you know, with adapting to school,' that that was really meaningful and important.

[00:54:42] And so, I think that that's something that's sort of on the backend of increased awareness that people cannot feel alone and be supported by their community and be supported by peers on this journey, if that makes sense, too.

Rebecca Whitney: [00:54:54] Yes, yes, absolutely it does. And it's incredibly important, that piece of support for families. And as we wrap up, is there anything else, Dr. Janell, that you would like to add as far as the CDC's preparedness plans for 2021?

Dr. Janell Routh: [00:55:16] Rebecca, thanks. And I think, I said it at the beginning, and I'll say it again. AFM is a priority at CDC. We are working incredibly hard to make sure that we are prepared for what may come this year.

[00:55:29] As we've talked, we can't stop an AFM outbreak from happening, but we certainly can put systems in place to inform and make sure people are kept up to date with the latest information that we're gaining from surveillance. And so, we have certainly since 2018 improved and strengthened those systems.

[00:55:51] I think, Emily, thank you for the shout out. We really have worked hard to improve the turnaround time with our case surveillance so that those members can be updated on a very regular basis. We have more neurologists now that participate in our expert panel. We have systems that make it easier to upload those MRI spinal images that are necessary for case classification.

[00:56:18] So, multiple things there have been put in place. We continue to put systems in place, again, to learn from every outbreak. And so, with new specimens that are sent to CDC, we continue to work on assay development. I know we talked about the fact that there's not a laboratory test for AFM, but certainly if we could develop something that would make it easier to identify children with AFM or to identify etiologies that are causing the syndrome, as Ben said, it would just lend it to improving our overall response and understanding.

[00:56:56] So, certainly the lab here at CDC is continuing to work hard doing that. And, you know, above all else, I'll say it one more time. I just think keeping in touch with those networks is critical. So, we talk to the AFM Work Group once a month. We have our AFM task force meetings once a month. Rebecca, you, when the SRNA are in regular communication, we are in touch with our state and local health departments through our ELC Vaccine Preventable Disease Grantees.

[00:57:30] We are keeping in constant communication so that at the first sign of an increase in enterovirus circulation or certainly an increase in cases, we're poised to really share that information forward.

Rebecca Whitney: [00:57:43] Great. Thank you so much.