

AFM Preparedness for 2020 and Beyond

You can listen to the audio of this talk at: <https://youtu.be/IFiKEdRaVFo>

Dr. Carlos Pardo: [00:00:00] Good afternoon. Thank you, Michael, for the introduction. Thank you for the organizers of the, SRNA symposium. It is great to be back here. And I say it is great to be back because, this has been an effort in the past 20 something years with the Transverse Myelitis Association and now with SRNA.

[00:00:20] So I was given the challenge to explain what is being in at this moment for acute flaccid myelitis and what is the preparedness that we have for acute flaccid myelitis. That is perhaps one of the major challenges and emerging, problems that we have in public health as well as in neurology in our century.

[00:00:49] So, what I like to do in the next 15 minutes is briefly outline the preparedness that we have for acute flaccid myelitis, what we have done in terms of unifying our opinion and views about diagnosis management, and explain a little bit about the public health effort as well as the future on management. Although again, some of those items are still work in progress. I'd like to disclose basically our major support, and I want to emphasize that the former Transverse Myelitis Association and SRNA has been critical for what we have done in terms of the understanding of myelopathies, myelitis in the past 25 years. Our colleagues at the Kennedy Krieger Institute have been a great partner as well for what we have been doing in terms of understanding all of these problems.

[00:01:48] So acute flaccid myelitis is probably not relatively a new problem. It's, acute flaccid myelitis is one of those disorders that we are recognizing in the past 10 years, and it is recognized because it is impacting young children and it's impacting entire families. And acute flaccid myelitis, as was explained this morning by Dr. Michael Sweeney in his presentation, is a myelitis, is one of the disorders that emerge, particularly in children after experiencing upper respiratory infections. And one of the particularities is the seasonality of the disorder. And it doesn't have a predilection for male or female patients, doesn't have a sex predilection. But it's very important to understand that this is a disease that's primarily affecting children between ages and one and 12, although there is description of patients above those age, and eventually some young adults as well.

[00:02:51] And the importance of acute flaccid myelitis is, for reasons that we still don't understand, despite members of the families that are affected with upper respiratory infection because presence of a viral infection mediated by enterovirus experience upper respiratory infection, only one subject particularly and one only one child may experience presence of myelitis. So that may suggest that there is some degree of host susceptibility or patient susceptibility for developing this type of a neurological problem.

[00:03:29] So, what is interesting, at least from our point of view, is that this is a disease that has been recognized in the past eight years, although it's very likely that we had cases of acute flaccid myelitis in previous decades, and probably we never recognized those problems. However, our

colleagues in Colorado and California back in 2014 recognized clusters of this disease. And after that, the acute flaccid myelitis has been recognized to produce outbreaks predominantly in the summertime and fall time. And the major outbreak actually was observed in 2018 when more than 238 patients experienced this disorder based on the surveillance by the CDC. This year so far until July 31st, we have recorded approximately 16 cases. And I believe that the low number of cases fortunately reflects the public health measures that we're taking for COVID-19 including the physical isolate distancing and the other public health measures like the quarantines that probably decrease the circulation of other viruses, like enteroviruses.

[00:04:59] Now, this is a very disabling disease. The numbers do not reflect the magnitude of the problem. The numbers basically may be just a statistic. But the impact of the disease in children, and the impact of this disease in families is overwhelming, particularly because almost 60% of these patients experience very aggressive disorders to the point that they are admitted to intensive care units, they experience significant respiratory problems and they are left with significant disabilities.

[00:05:40] Dr. Sweeney mentioned this morning, that the magnitude of the disease in 2018 was very important more than 238 patients this year. The disease has been seen sporadically in some states, particularly in Texas and California and other states, but fortunately, the magnitude of the problem is not necessarily as overwhelming as in 2018. One of the concerns that we have is this disease is associated with a viral infection, particularly enterovirus D68, that produces a specific damage of the spinal cord as it was explained this morning. But what I like to mention is that a very large percentage of patients, almost 60% of the patients actually experience aggressive disease and are admitted to the Intensive Care Unit. And frequently, many of them, almost a quarter of them, are left with significant problems with quadriplegia. And, this is important to understand because these are going to be long-standing neurological problems and disabilities, that not only the patient but also their families and health care providers are going to be basically dealing with over the next several years.

[00:06:54] So it's extremely important that we understand what is going on with acute flaccid myelitis. And that is one of the reasons we may need to focus in many efforts, and the effort is first to make people aware about the disease, to have a better diagnosis, to establish better treatments, and perhaps to target long-term management that allow these children and families to have a better quality of life.

[00:07:22] So in the next few minutes, what I'm going to explain is what we have done so far to answer those challenges; the challenge of what is needed to confront the monster of acute flaccid myelitis and there are different fronts for preparedness about this. Number one is, from a healthcare point of view, is just to make sure that we improve diagnosis, we improve detection, we improve the surveillance for this disorder, and we educate the healthcare providers and all healthcare systems to establish a better diagnosis. And obviously, we need to initiate a plan of research that allows us to understand acute flaccid myelitis with the final purpose of facilitating a better family support and treatment of these patients.

[00:08:16] So one of the efforts that we have done in the past two years, is basically to establish a network of collaboration around the country and around the world that is going to be focused on a

model of horizontal collaboration to establish consensus for clinical diagnosis, management and research. And this was the wave of our group that is the Acute Flaccid Myelitis Working Group that was established back in September of 2018. Just to answer those challenges, to establish that horizontal collaboration. And so far at this moment, we have many research centers, clinical centers, and institutions around the United States and Canada who are part of this effort of the Acute Flaccid Myelitis Working Group. One of the major challenges that we took was to establish a better consensus on diagnosis.

[00:09:18] And, these actually led to a very interesting discussion and in the next few weeks one of our efforts probably will be available in the public domain. And this is basically the consensus for clinical diagnosis of acute flaccid myelitis that was discussed by the Acute Flaccid Myelitis Working Group in collaboration also with international partners.

[00:09:46] And this is in process of review, but what I like to emphasize briefly here is two different aspects. Number one is we have outlined the better approach for diagnosis that will include not only the clinical assessment with identification of the critical elements of the clinical presentation of acute flaccid myelitis, like the presence of acute onset of limb weakness, but also elements of examination to have a better documentation of the neurological exam, to have a documentation that the patient is experiencing a lower motor neuron syndrome. And in addition to those two elements, the elements of the magnetic resonance imaging to establish the presence of damage of the spinal cord, specifically in the gray matter, the structures, as well as analysis of spinal fluid analysis.

[00:10:42] I don't have too much time to go through the diagnostic criteria but what we like to emphasize and this again, this is going to be published hopefully very soon, is that we outline the criteria for establishing the definite diagnosis, the probable diagnosis, and possible diagnosis that allow a better identification of patient with acute flaccid myelitis and obviously, a much better treatment of the disorder.

[00:11:09] In the same way, the group has reached a better outline of the recommendations for acute management, for inpatient rehabilitation, and the use of strategies to improve the quality of life of all of these patients. And again, I think that this is going to be a very valuable tool that is going to provide guidance for diagnosis and management in the future. So this has been basically a work by many colleagues around the United States and Canada and the world to basically reach this consensus.

[00:11:48] Now, I want to emphasize that acute flaccid myelitis need to be clearly identified in the context of myelopathies in the pediatric population. And I like to emphasize that we are seeing acute flaccid myelitis, but we shouldn't forget that children are affected by other type of myelitis. I like to bring the experience that we have in our center in the past eight years, in which, in addition to acute flaccid myelitis that comprise approximately 30% of the cases, there is also patients and children that are affected by other types of myelopathies, from autoimmune myelopathies like neuromyelitis optica or MOG associated disorder, to vascular myelopathies and other types of non-AFM infection related myelopathies. So we shouldn't forget that children have other type of myelopathies that we need to pay attention in the future, particularly to establish a better differential diagnosis.

[00:12:51] It is important also to emphasize that in the pediatric population, particularly below age 12, acute flaccid myelitis takes a very large percentage of the cases. Although, it is important to clarify that this sort of like vascular myelopathy and autoimmune myelopathies may occur during that patient spectrum as well.

[00:13:12] So, what is on the road for understanding acute flaccid myelitis? And is a list of a lot of items that we need to develop and answer correctly.

[00:13:28] First is, what is the role of viruses in pathogenesis? We have already a main suspect that is the enterovirus D68. It is extremely important that we understand if that is the only virus or there are other viruses that may be associated with the pathogenesis of that disorder.

[00:13:47] We need to understand also how the immune system is involved in acute flaccid myelitis. We put all the guilt on the role of the virus, but we shouldn't forget that the immune system has extremely important role in pathogenesis. And we need to emphasize in the diagnosis of these patients, and this is one of the efforts that we have basically established in the past couple of years. And we need to understand what are the factors that are associated with prognosis and outcomes, as well as strategies to improve treatments as well as outcome in, in this patient population.

[00:14:24] And finally, we need to develop strategies for prevention and particularly to see if we are able to see a vaccination that may prevent the development of these. So in terms of education, I will invite all of you to take a look of the SRNA website as well as the Acute Flaccid Myelitis Working Group information based on the acute flaccid myelitis symposium that was presented in June and July. And there is a very good collection of lectures about the preparedness for acute flaccid myelitis. And if you Google AFM Virtual Symposium on YouTube, you immediately are going to find a very nice collection of lectures that are focused on different aspects of preparedness for acute flaccid myelitis.

[00:15:21] Now, from research point of view, at this moment the National Institute of Health, particularly the National Institute of Allergy and Infectious Disorder, is supporting the Natural History study of acute flaccid myelitis that was launched this year, in response to the need of better research for acute flaccid myelitis. At this moment, there are 35 centers around the country that are recruiting centers for evaluation and assessment of patients and the clinical profile, as well as biological samples from patients with acute flaccid myelitis. And this effort basically includes the recruitment of patients with suspected acute flaccid myelitis that are less of 18 years of age that are able to be followed for at least a period of one year to determine what are the clinical profiles as well as determine what are the main characteristics of the natural history of this disorder.

[00:16:28] And along with the recruitment of patients with acute flaccid myelitis, there is going to be a long battery of tests - clinical and biological tests - just to establish a better understanding of the natural history of the disorder. This is in the public domain, and if somebody is interested in learning more about what is being done in this patient population. Along with the recruitment of patients with acute flaccid myelitis, there is going to be recruitment of a control group that is going to be based in the recruitment of patients without clinical symptoms of myelitis, but a patient that have basically, or are part of the household contact of the child that is affected by acute flaccid myelitis. In

other words, siblings or other household contacts that will facilitate understanding of the genetic background, immunological background and even virology background of many of these patients. And they are going to have not necessarily an extensive battery of testing, but just a very selective group of tests that will allow us to answer basic questions about clinical profile, virology, and immunology.

[00:17:44] There is an interesting question about acute flaccid myelitis and genetic susceptibility. And the issue of genetic susceptibility is something that has generated a lot of interest in the past several years since the initial outbreak of acute flaccid myelitis. One of our colleagues at John Hopkins, Dr. Priya Duggal has been leading the effort for the national level with a case control study for understanding the genetic susceptibility question. And if you are interested in learning more about this, the SRNA podcast series has a very nice interview with Dr. Duggal about that study.

[00:18:25] So what about treatment? And the treatment is obviously an area that needs a lot of effort. And we know in the past eight years, that so far, many of the treatments that we have used previously in acute flaccid myelitis have been not necessarily very effective. We know that many of the treatments that traditionally were used in myelitis were not necessarily effective for rescuing patients with acute flaccid myelitis. So there is a lot of effort for understanding how we are able to develop new antiviral medications that basically treat enterovirus D68. And in that effort, obviously, there is an urgent need for developing animal models for testing those antiviral medications. There is an urgent need for developing vaccination for enterovirus D68 and particularly efforts to improve the rehabilitation of these patients and other strategies like understanding what is the role of nerve transfers or tendon transfer for rescuing limbs and function in this patient population.

[00:19:35] I am going to briefly mention this study. This is a study by Matthew Bock, who is a pediatric infectious disease specialist who recently published the identification of a very interesting approach for treatment that is the use of human antibodies that neutralize enterovirus D68, that eventually may protect in the future for further development of complications associated with infection. So this is the technology that is being investigated at this moment, and it is still in a very early stage of analysis because it's basically on animal models studies. The future is probably going to be focusing on identification of these immunological measures that neutralize the viral infection and prevent in better way the development of acute flaccid myelitis.

[00:20:28] So in summary, what we need to do in the future is, number one, improve our awareness about AFM, improve our diagnosis and make sure that we establish the proper treatment and chronic treatments to improve the quality of life of patients and actually facilitate the better life of many of the families. This is not an individual disease, this is a disease that affects the entire family because of the magnitude of disability that many patients experience. And I think that the Acute Flaccid Myelitis Association and the families that are around SRNA are doing a great job just facilitating the education about this disorder.

[00:21:10] So, thank you so much again for the invitation and for facilitating more education about acute flaccid myelitis.