

Live Q&A Session

You can watch the video of this event at: youtu.be/CTiyHqntlXY

[00:00:05] **Krissy Dilger:** Hello, everyone. Thank you for joining us for this AFM Together event. We're now in the Q&A portion of the event with our two experts, Dr. Grace Gombolay and Dr. Cristina Sadowsky. So, I'll just thank you both for joining us and taking time out of your day to answer some questions for us. I know our community members really appreciate it. So, to start off, we will just start really basic and ask what is acute flaccid myelitis, and what are the diagnostic criteria for AFM? Dr. Gombolay, can you start us off?

[00:00:44] **Dr. Grace Gombolay:** Yeah, absolutely. So acute flaccid myelitis is where patients come in with acute flaccid limb weakness, meaning that they're weak, they can't move their arms or legs. When they're flaccid, meaning that there's low tone. And then myelitis means it's a specific word that means inflammation in the spinal cord. And so typically, what happens is that these patients present after sometimes there's a week prior of having cold symptoms, sometimes gastrointestinal symptoms such as like a stomach bug, and then they'll come in with developing weakness. Oftentimes, it takes a few hours to a couple of days to have that weakness. It's not something that happens within five minutes or 30 minutes.

[00:01:30] If it's a sudden onset, then we have to think about other causes for the weakness. And then in terms of diagnostic criteria, generally, what we look at is the clinical symptoms, the timing of symptoms and then we get imaging. So that would be magnetic resonance imaging or MRI of the brain and the spinal cord. And we definitely look at the spinal cord to look at those features consistent with AFM. So that would be looking at the spinal cord and seeing if the center part of the spinal cord, which is where the gray matter, which is where the cell bodies like our neurons, and see if that is affected. And so, if you're seeing a patient who has or someone comes in with flaccid weakness, I mean, they have low tone, they're extremely weak and then you see the evidence of the gray matter involvement on the spinal cord, that's when you start thinking about AFM.

[00:02:28] **Krissy Dilger:** Great. Thank you and Dr. Sadowsky, do you have anything to add or?

[00:02:30] **Dr. Cristina Sadowsky:** I think that a lot of practitioners will add CSF criteria. So, it's part of the workup. So, a lumbar tap will be performed and there are specific findings in CSF with some cell count that are predominantly lymphocytes and definitely no growth. There is this hope that if we get a very early sample, we would maybe be able to grow a pathogen which would be a virus. But to date, that hasn't occurred yet. We still don't know if AFM is -- we would be able to grow the pathogen or the reaction in the cord is actually a reaction to the pathogen outside of the central nervous system. So, we don't know if it's an infectious pathology or if it is an autoimmune reaction of the body to it, but CSF is important to also do a differential diagnosis with other pathologies that could present similarly.

[00:03:50] **Krissy Dilger:** Great. Thank you. This kind of touches on what you just talked about. But our next question is what causes AFM or what is known about the cause of AFM? And are there any predisposing factors that have been identified thus far? Dr. Sadowsky, can you start us off?

[00:04:10] **Dr. Cristina Sadowsky:** Well, the general consensus is that enterovirus is the main pathogen, although there are some other three or four or five that are considered possibilities. But enterovirus D68 and A71 are the ones that are more prevalently associated with. And the association has been done epidemiologically, meaning that the cases of acute flaccid myelitis have occurred in periods in which enteroviruses were prevalent, were ramping through the community. There were some growth identification of the pathogen, but again, not in the CSF but in some other samples, that could be respiratory, that could be GI stool, and so forth, but that's the current that I am aware of. So, I'm going to allow my co-panelist to add.

[00:05:21] **Dr. Grace Gombolay:** Right. I agree with that. I think right now there's an association which means that there are things that happen at the same time and it's not quite, we haven't proven causation, meaning that the enterovirus causes AFM. Although we do think that there is likely a relationship with that and then there's been a few studies hinting that it may be more of an autoimmune cause. Although we still don't know, like Dr. Sadowsky said earlier, we still don't know if it's direct, the virus actually directly invading the cells and causing injury versus the immune system responding to that virus.

[00:06:04] But there's some evidence to suggest we know that the immune system has an involvement because there was a study looking at antibodies to enterovirus and there was the vast majority of patients who had AFM, had positive antibodies to enterovirus in the spinal fluid. So, unfortunately, that testing is more on a research basis, as opposed to a clinical basis. It's not something that we can do clinically quite yet. But there is that suggestion that definitely there's an immune system component but whether it's purely immune system versus the immune system and the virus is still yet to come in.

[00:06:40] **Krissy Dilger:** Okay, thank you. This next question kind of leads into what you were just talking about the research that's being done. So, is there research being done currently on AFM? And are there any clinical trials that people may be aware of or ongoing? Dr. Gombolay, do you wanna start?

[00:07:01] **Dr. Grace Gombolay:** Yes. So, there is definitely a lot of work being done in AFM just because we want to really understand this disease. We know that it can be, even though it's rare, we know it has a lot of impacts on patients and families. So, it's one of those things that we've been doing. One of the major studies is there's a lot of different groups actually, for example, there's the Acute Flaccid Myelitis Working Group, the AFM Working Group, which is headed up by Dr. Carlos Pardo, who's from Johns Hopkins. He's really assembled a really wonderful group of many, many individuals from many institutions across the country in different subspecialties. And that's really come together to really tackle this problem.

[00:07:43] And then that, the AFM working group published a paper recently in Lancet discussing not only some of the diagnostic criteria for AFM but also considerations for how to manage a patient, including how to evaluate a person with AFM. In addition to that, the NIH has actually put some funding into this also. There is a multicenter NIH AFM Natural History study that's ongoing. There are multiple sites across the country that are enrolling patients with this study. And the idea is we just want to understand what happens. And so, it's everything from clinical symptoms, we enroll household contacts. So, if there's any siblings or other people in the house, who we think have been also exposed to the same pathogens, but don't have AFM, we're trying to figure out why that happens. Why do some people get AFM versus not? It also includes MRI, the imaging features and then they also collect biospecimens, which includes blood and spinal fluid and respiratory, saliva tests, and urine and stool tests. So, we're trying to collect all of these biospecimens to really try to get at what's happening in this disease.

[00:09:02] **Krissy Dilger:** Oh, that's a lot going on. It all sounds great and just happy that so much work is being put into understanding this disease better and hopefully treating it more effectively. Dr. Sadowsky, did you have anything else to add? Or Dr. Gombolay cover it all?

[00:09:22] **Dr. Cristina Sadowsky:** Well, yeah, because the prospective studies, the big NIH study is the one that is, I think the one that will tell us a lot more about the AFM and everything else is kind of retrospective data analysis or prospective restorative activities interventions, people looking at case cohorts and I'm going to say this is the state of the art right now because there are only hundreds, this is a very orphan disease which SRNA is used to dealing with. And there are only hundreds, several hundred patients diagnosed with AFM in the world. So yes, there is a prospective data collection study which is dependent on the disease actually occurring. And luckily, since 2018, we didn't have a big number, a big one of those every two years peak of cases. But that kind of also hampers the prospective research. But that doesn't mean that the retrospective analysis doesn't give us information about what happened to these children.

[00:10:43] So there are numerous papers that look both at the viral etiology. There are papers that look at the role of EMG, then there are retrospective case series looking at outcomes following diverse intervention including nerve transfers. So, all of that literature contributes to building this database where we can go and ask a question. And I am encouraging everyone who's there and I don't know, I know that the community has a very big influence on the medical professionals. Any case is important when we're dealing with 600-something cases in the world of a disease. So, publishing a paper about one case or 10 cases is important because, in the end, we can look at meta-analysis and umbrella meta-analysis that we can pull all that data together and that Dr. Gombolay was saying about the AFM Working Group. Dr. Pardo has done this wonderful, wonderful bringing collaboration with everybody.

[00:12:09] We have people from South America, from Europe, from Australia, from Asia, everybody's contributing because we need a very large catchment area in order to understand what this is. And listen, if this disease doesn't occur anymore, I'm happy. But even those 20 to 30 cases that can happen as a baseline might not be related to enteroviruses, might be related to something else. We still need to know about that. And I'm bringing in the CDC here because they are doing a great job in informing the public about it. And again, I'm reaching out to the community because this is the voice that is heard the most.

[00:13:03] **Krissy Dilger:** Great. Awesome. Thank you. Okay, our next question is about vaccines. So, is there a vaccine in the works for enterovirus or EV-D68? Dr. Sadowsky, do you wanna touch on this?

[00:13:20] **Dr. Cristina Sadowsky:** Well, so I'm going to say that I am not the specialist in it, but I understand that there is a vaccine. I think there are several vaccines that are being worked on, but there is one that I know it's a little bit closer to, but I don't, I don't think that data is yet published and I am going to say that I can't say more than this, but there are several vaccines that I am aware that people are working on.

[00:13:55] **Krissy Dilger:** Awesome. Thank you, Dr. Gombolay, is that similar answer that you would give or?

[00:14:00] **Dr. Grace Gombolay:** Yes, exactly. There's nothing available right now, but there are definitely several groups who are working on developing such a vaccine.

[00:14:10] **Krissy Dilger:** Well, that's really exciting, and excited to learn more about that once that data is made publicly available. Okay. Our next question again has to do with vaccines. This was from a parent. I'm afraid to continue vaccinations for my child. I've heard stories of vaccines causing AFM and TM in kids. I don't want to go through this again. Can the polio vaccine cause AFM or any other vaccines? Can they trigger an AFM attack? Dr. Gombolay, do you wanna address this?

[00:14:45] **Dr. Grace Gombolay:** Yes, absolutely. So as a neuroimmunologist, I see children who not only have AFM, but other autoimmune conditions that can be associated. Again, it's that association. We know they occurred around the same time. And so, to say that the vaccine caused it is really hard to say. But since it

occurred around the same time, we would definitely want to explore that relationship. It's rare, but I've definitely seen a few patients who we think that there is a temporal relationship with a vaccine, not only with AFM but also Transverse Myelitis or TM. And that it can happen, but I think we have to individualize this discussion for each patient and individual. So, what I mean by that is that there are many, there are millions of children who get these vaccines. And then, fortunately, these conditions are rare and don't occur in most children.

[00:15:51] But even though it's rare, I always say, you know, even if something is 0.00001% if it happens to you, it's 100%, right? And so, even though we know that there could be this potential association of vaccines with AFM or TM or other conditions, I still recommend administering vaccines to children just because it's at risk versus benefit. For me, the risk of having a serious infection outweighs the risks of potential vaccine-related complications. And I will say personally, I am a mom, I have three little ones. I have a five-year-old, a two-year-old, and a four-month-old. And so, despite seeing children in my clinic who I know that, you know, we sort of say, okay, it may be likely the vaccine triggered this in your child. I still am comfortable vaccinating my own children just because that risk of, that serious infection could cause more harm.

[00:16:31] And then just to answer the question about the polio vaccine causing AFM, I'm not aware of the polio vaccine causing AFM. There are definitely rare instances where the polio vaccine resulted. But this was if it was a live attenuated virus, meaning that it was a live virus that they try to make weaker, but in that particular patient who received that particular vaccine, and it was probably related to a lot of factors including the immune system factors in that particular person. The virus became more active and then caused poliomyelitis which can look like AFM or AFM is an umbrella term for poliomyelitis. But we really do recommend the polio vaccine especially if it's the inactivated version just because to prevent poliomyelitis, because poliomyelitis is also quite severe and recovery from that is pretty poor also.

[00:17:53] **Krissy Dilger:** Dr. Sadowsky, did you wanna add anything?

[00:17:55] **Dr. Cristina Sadowsky:** I don't have anything to add to a neuroimmunologist and a mother of little children's opinion. I will say that from a humanitarian global perspective, immunization saves lives. So, I know that when we're looking at each disease and medicine, we look at a patient-centered image but then with infectious disease, we also have to look at the rest. I was just listening to NPR yesterday that there are cases of malaria in the United States, and malaria has been eradicated in the United States but now some people in Texas and Florida contracted it because it has been brought in and it hasn't been contained, and that's the story with infectious disease. If one case of infectious disease occurs, it affects everybody around. Maybe that's another reason to immunize your children. I do have grown-up kids and they are fully immunized.

[00:19:19] **Krissy Dilger:** Thank you. That's another great perspective. So, I guess another, we have two questions kind of related to poliomyelitis and AFM and the relationship between the two. So, I'll kind of just combine them. Someone asked, how do we know that recent cases of polio aren't really AFM? We also had someone submit this question. I don't understand the difference between AFM and poliomyelitis. How is AFM different from polio or isn't AFM just a new name for Polio? I don't know if either one of you feels more comfortable addressing this question. Dr. Gombolay if you want -- see you're nodding your head.

[00:20:02] **Dr. Grace Gombolay:** Yeah. So, I can do it because I think I may have caused some of this confusion. So acute flaccid myelitis, I'm just going back to that definition is the syndrome where someone comes in with flaccid limb weakness and we see inflammation in the spinal cord and/or in the spinal fluid. But I will say, so AFM is this large umbrella and there's probably multiple causes that fit under this umbrella of AFM. Poliomyelitis being one of them.

[00:20:28] And then if you have poliomyelitis, which is one subparts of AFM, that's when you actually have the polio virus that's been isolated, and we know that the polio virus triggered your AFM. But because of the Polio vaccine in the United States, the majority of cases of AFM will actually not be related to polio and that's why we're trying to investigate what are these cases looking like because they can look like poliomyelitis but are not caused by the polio virus. Dr. Sadowsky feel free to elaborate and clarify this.

[00:21:08] **Dr. Cristina Sadowsky:** Yeah. You didn't create the confusion. I think you called it at the beginning when these cases were gaining prominence, we call it the polio of the 21st century and so forth. But yeah, it's a placid paralysis that has an acute onset. We call AFM this specific occurrence since 2012, 2014 every other year with some baseline yearly occurrence, but it's flaccid paralysis with acute onset and polio is part of it, but it has an etiology. We know who does it and we know how to treat it or prevent it. Prevent it, not treat it.

[00:21:58] **Krissy Dilger:** Gotcha. Well, thank you. And I think, yeah, you didn't cause the confusion. I think these questions are ones that we get quite often. So, thank you for addressing them. Okay. Moving on to another topic that we get questions about a lot. Has COVID caused any AFM cases? Dr. Sadowsky, I don't know if you wanna address this or pass it on to Dr. Gombolay. Either one.

[00:22:27] **Dr. Cristina Sadowsky:** So, I'm going to say I personally am only aware of COVID causing transverse myelitis or being associated with because again it's a temporal association. And if I'm going a little bit further into this, when I say transverse myelitis, and I don't call it acute transverse myelitis, I'm referring to the fact that it has a different image on the MRI and is associated with more spasticity and definitely not in pediatric population in adults. So that's my knowledge.

[00:23:17] **Dr. Grace Gombolay:** Yes. I agree with Dr. Sadowsky. There are probably one or two cases here and there that have been published with a child or a patient had COVID and then developed AFM. But to say it caused it, it's hard to say. But I think what's been interesting like Dr. Sadowsky alluded to is that generally, AFM has had this every two-year periodic. So, when we first noticed about it in 2012, there was a bump in cases in 2014, 2015 was quiet, increased again 2016, '17 was quiet again, 2018 was actually the last time we had this peak. And so, we were expecting to have this peak in 2020 and in 2022, but actually, the number of cases has been very few sorts of that just that 20 to 30 per year.

[00:24:08] And that's despite many people getting COVID. I mean, even though I do think that potentially COVID could be related to AFM, I think that with the number of people who have gotten COVID over the past three years since the pandemic happened, but despite seeing very few cases, I just don't see that COVID is gonna be the culprit. Again, it may be in a handful of patients here and there. But I don't see that being the main driver of AFM.

[00:24:37] **Dr. Cristina Sadowsky:** I think that it's important to mention that COVID is associated with long COVID and that occurs in children, but long COVID is not characterized by paralysis, but the extreme fatigue and the autonomic dysfunction that's associated with the long COVID could in the general public, not in the medical professionals, but in the general public could put it into the same category. But definitely, if there is any of that reach out to your pediatric neurologist because they're different and the long COVID has symptomatic treatment that's very effective.

[00:25:30] **Krissy Dilger:** Got it. Thank you. So, our next question is about classifying cases. What qualifies as a reported case of AFM by the CDC? How does CDC's criteria for AFM differ from how a neurologist may diagnose AFM? Dr. Gombolay, do you want to start us off on this one?

[00:25:54] **Dr. Grace Gombolay:** Yes, absolutely. So, I am actually part of the panelist of neurologists who reviews cases for the CDC. So, I can comment on what our experience has been. So, what we ask from the CDC is that if a clinician suspects that a patient could have AFM defined by the acute flaccid paralysis and if on the spinal cord imaging, there's predominant gray matter involvement, meaning that even though that other parts of the spine, because in the spine, you have both gray matter and white matter, even if a little bit of white matter is involvement. If it looks like that more grey is involved than white, definitely these cases need to be reported to the CDC. And now that happens is that the clinician will report it to the local state health department who then coordinates with the CDC. They send us the information, the images, the MRI images, and then any biospecimens that ends up at the CDC.

[00:26:43] I will say, so, the thing is that our classification takes time to get back to the clinician. So, this is not a purpose in which we're making the diagnosis for the clinician because clinicians need to make that diagnosis and treatment in real time whereas our processing or review process takes time before we come back. And what we're actually doing is what we call as disease surveillance. We want to figure out how often is AFM occurring in the community. What are the rates of AFM in the community? And then once we look at that, we're actually doing a secondary project now where we go back two or three years later after someone who said, okay, the CDC says you've been classified as AFM, we don't know what your actual clinical diagnosis at the time. We just know you fit this criteria of the flaccid paralysis and the grey matter involvement.

[00:27:34] Now we're going back looking at those cases and saying, okay, now that we've gotten all of this testing back, what was the actual diagnosis for each of these patients? Did it end up being transverse myelitis? Did it end up being other antibody-mediated syndromes like anti-MOG or myelin oligodendrocyte glycoprotein or aquaporin 4 related neuromyelitis optica spectrum disorder? Was there an infection involved? Did we realize it was a spinal cord stroke? So, there's lots of different entities that can look like AFM. And then we try to do this investigation later on of saying, okay, even though the CDC says you're classified as AFM, we're gonna -- have you still depend on what your local clinician, your neurologist says that you have, have them treat you accordingly of what they think the diagnosis is. But on the back end, we're trying to figure out how often does AFM occur and then what constitutes AFM, so we can start parsing out what are the different causes for this entity.

[00:28:32] **Krissy Dilger:** Got it. Well, that was a great explanation and the perfect person to ask. So, thank you for that. And Dr. Sadowsky, was there anything you wanted to add to that?

[00:28:41] **Dr. Cristina Sadowsky:** Nope.

[00:28:41] **Krissy Dilger:** Awesome. So, this next question is, I guess a little bit more about long-term expectations. So, Dr. Sadowsky, if you want to start us off, is it likely that someone will regain any more function after 10 months from diagnosis?

[00:29:01] **Dr. Cristina Sadowsky:** An emphatic yes. So now that we end up seeing, we have almost 10 years' worth of experience with the cohort in 2012 and so forth. We see that there are ongoing changes in function and it's hard to parcel them out because every parent does a lot to try and improve the neurologic and day-to-day outcome of their child. But as a general statement and what we've seen is that children improved and reached functional outcomes that us as professionals did not expect with the level of muscle weakness that they had. I can't say that that's related to a specific intervention.

[00:30:06] I know that there are some studies that are showing that well, if you have these specific characteristics at the beginning, again studies, these are case series. If you have the specific characteristics, if you have

more involvement of this, you're more likely to not gain this function or if you had a specific nerve transfer, you're likely to improve this specific function. But these are all very case-specific. Taking it as an umbrella, I can tell you that parents that didn't do anything except rehabilitation for their children report as they grow, improvement in motor and day-to-day function and I'm going to Dr. Gombolay add to that.

[00:31:06] **Dr. Grace Gombolay:** Yes, I agree with that. I'm always pleasantly surprised of how kids recover because most of these patients are kids, there are some adults who can have AFM but generally, if this occurs in children, I'm always pleasantly surprised to see how children gain their function. I think getting involved with those interventions as soon as possible really helps. But one thing that we do know especially with rehabilitation, it might seem like simple exercises, but what you're doing is you're training the muscles, you're training the nerves, you're stimulating potential growth factors within the nerves and in the spinal cord. So even if it may not seem like it's helping right now, you never know the long-term benefits. So just really making sure involved in those therapies can help.

[00:31:52] **Dr. Cristina Sadowsky:** I do wanna -- I forgot to mention that it's a good idea to involve your neurosurgeon or plastic surgeon, the ones that do the nerve transplant in your community early in the assessment of the cases because early involvement leads to a better planning. And there are some cases that would benefit from earlier than maybe postulated transfers. And I'm talking nerve transfers, not so much tendon transfers, but I know that there is this tendency of and I'm a rehab person. So, I'm always like activity, activity, go ahead. Let's do the exercise. But I do involve my very friendly neurosurgeon because I know that together we can have a better plan. So, we can take on those small changes or lack of changes that we expect to occur as we apply the intervention. So, I'm kind of supporting an assessment in the first three months. Just bringing those specialists, the electromyographer, which is usually a neurologist or a physical medicine or rehabilitation specialist and the neurosurgeon or the plastic surgeon, the person in the community, the surgeon in the community that does the transfer. So, bringing them early, even if the surgery will never occur.

[00:33:28] **Krissy Dilger:** Okay. Great. Yeah, I think that's good advice and I agree wholeheartedly. Okay. Our next question, is it possible for a child diagnosed with AFM to later be changed to TM or MOG? We got another question. I'm not sure if it's from the same person or not, but how might this change or differ if there's also white matter involvement in this final card? Our doctor says they still aren't certain if it's AFM or TM. Is it possible to have both? So, I mean, I think these are all kind of related. Dr. Gombolay, do you wanna address this or speak to diagnosing --

[00:34:07] **Dr. Grace Gombolay:** Yeah. So sometimes, especially in the early stages, it can be really hard to tell what a patient has. I do base it on not only the imaging but the clinical symptoms because you can have both. So, you can have somebody with really early transverse myelitis who come in with flaccid weakness. So, they look like AFM, or you can somebody who comes with AFM who also has a lot of edema in their spinal cord. So, they'll have some of those what we call upper motor neuron signs. So, it involves the white matter tracts in the beginning, but it's over time that you'll see and so getting subsequent imaging can sometimes help and then some sort of looking at the clinical portion.

[00:34:45] Generally although this is patient dependent, the way I look at it is that if a few weeks out from the onset, if a patient remains persistently flaccid, and then it's hard to get reflexes from them and then we get the special electromyography or nerve conduction studies, the special needle test to look at the function of the nerves and the muscle and it shows that low nerve function and that the nerves have been damaged or that the gray matter is involved, that's more AFM. Whereas in transverse myelitis patients, even if they come in flaccid in the beginning, over the next few weeks, you'll see them develop more of that spasticity, more stiffness, more brisker reflexes. So, whenever I tap on the patient's knee, it's really brisk meaning that it kicks

out really fast as opposed to minimal response so that can happen. Generally, and that's one of the things we're trying to figure out. What's that line between AFM and transverse myelitis? If it's more grey matter involvement, then we tend to say it's more AFM.

[00:35:46] If there's white matter involvement, but how much is too much white matter involvement? When does it become transverse myelitis? So that may make it challenging and as opposed to the MOG diagnosis or the aquaporin-4 NMOSD, yes sometimes I can come back later because you could have somebody who comes in with MOG antibody-associated disorder or MOGAD and they look like AFM in the beginning. But it's not until their MOG antibodies come back. Sometimes it can take up to four weeks, sometimes -- Usually it's faster, but it can take up to four weeks. It's not until the MOG antibodies come back that you say, oh, this is MOGAD. My experience with MOGAD and aquaporin 4 is that you fit that transverse myelitis, seeing that upper motor neuron risk. There have been a few cases where someone thought they had AFM with a flaccid weakness and then later on had the antibody testing that was positive.

[00:36:38] **Krissy Dilger:** Got it. Yeah. Okay. Thank you. Dr. Sadowsky, anything to add?

[00:36:45] **Dr. Cristina Sadowsky:** No. Well, you know, there's always a controversy about this and it's an ongoing conversation. I think my -- the point that I want to make is that in medicine, there are very few things that are black and white, we call them syndrome a lot because it's an association of things and science is ongoing step-by-step answering questions, but it's an ongoing process. So be patient with us in the medical community. Sometimes we don't have that black-and-white answer, but each one of us is working to get that answer. And as science and knowledge progresses, we add, we might change. That doesn't mean that we were wrong at the beginning. We just didn't know. I know this is a little bit of philosophy because it applies to a lot that occurs in science these days.

[00:37:54] **Krissy Dilger:** Gotcha. We kind of addressed the next question already a bit, but I'm gonna throw it out there just in case there was anything you wanted to add. Are there best practices when it comes to starting physical therapy or determining if surgical interventions are necessary after AFM? Dr. Sadowsky, I know you've talked about this a bit already, but if you wanna add anything.

[00:38:21] **Dr. Cristina Sadowsky:** I'm going to refer everybody to the Lancet paper on acute flaccid myelitis. The best practices for physical therapy are start early in the ICU. The child is in the pediatric ICU, start early with that intervention and kind of follow the progression. Activity is important for disuse atrophy, for paralysis, for the fact that children have respiratory dysfunction and initially autonomic dysfunction. So, all of that is being addressed with activity. Again, surgical intervention, I kind of said bring everybody into the fold because you know, having more minds to discuss, one case is definitely better than just not having that. Again, go back to Lancet. That is kind of the guidelines for now and then look for centers of excellence when it comes to having to having a child treated for an orphan disease.

[00:39:29] That doesn't mean that you have to only go to a center of excellence but look for the knowledge that emanates from a center of excellence and COVID has done a lot of damage to us, but it did add telehealth or better access to telehealth. So, reach out to the centers that are known that publish the papers about AFM, ask questions, be proactive. If you can travel there, fine. But that's not a requirement. The requirement is to gather the information and bring into your community because more individuals, health care professionals that become familiar with treating a child with an orphan disease, the better the outcomes are for everyone.

[00:40:23] **Krissy Dilger:** Agreed.

[00:40:25] **Dr. Grace Gombolay:** Yeah, if I can just -- yeah, I agree with that. I just want to really emphasize that if you don't have someone local in your community, go ahead and reach out to the experts. There are so many people across the country who are really kind, love talking to patients and families and helping them. And even if it's one of those things where you can travel once every couple of years to get that assessment, I've done this a lot for patients and families where I'll see a patient and family once a year, once every couple of years, but I'll work with their local neurologists or local practitioners just to help them guide their treatment. And so that's one of the things that we can definitely help with.

[00:41:09] **Dr. Cristina Sadowsky:** We should plug SRNA because SRNA does this day in and day out.

[00:41:16] **Krissy Dilger:** Yeah. If anyone reaches out to us, we definitely are happy to help connect people with experts like yourselves. And also, we have a medical professional network on our website that you can check out and see who has specialties and what area they're in and contact information and such. So, yeah, but thank you for that point because I think that's an excellent point. Okay. Your next question is about post-polio syndrome. So, this is a concern for adults and seniors who have polio as a child. Is this a concern for kids with AFM? And can you even just define what post-polio syndrome is? Dr. Gombolay if you wanna start?

[00:41:58] **Dr. Grace Gombolay:** Yeah. So, post-polio syndrome is for those patients who have had polio as a child and then it's usually, poliomyelitis is a one-time attack. We know it's from the poliovirus actually attacking the spinal cord and affecting the neurons in the spinal cord which causing the -- that feeds the muscles. And that's why we get the weakness. But it's usually a one-time thing and then their symptoms and everything are stable for a period of time. But there's actually a subset of people who've had polio when they were a child and then when they become adults, they start getting worsening symptoms. And it tends to not be this more acute attack where everything comes on within a few days, it takes over months and years. They're realizing they're having worsening disability, for example, more trouble with motor movement and that sort of thing.

[00:42:49] We don't know what causes post-polio syndrome. We don't think it's from reattack from the polio virus or reactivation, but we don't know. We don't know if it's your immune system will suddenly decide to respond to something and start causing symptoms. And so, we don't really know what's triggering it or what's causing it. So far -- I'm curious with Dr. Sadowsky's experiences and so far, I have not seen this in the children I've seen with AFM, nor have I seen it reported in the literature. But the post-polio syndrome occurs, we're talking decades, sometimes 10 to 20 years from poliomyelitis whereas we haven't had that follow-up yet. We've had a decent amount. So over 2023 so close to 10, 11 years, but we're still haven't had that decades of follow-up. So, my hope is that this doesn't occur with the children with AFM, but I don't think we know yet. I'm curious what Dr. Sadowsky's experience has been.

[00:43:48] **Dr. Cristina Sadowsky:** Yeah, I agree with the AFM we have no experience and we're not expecting it yet. As you said, it requires decades and the post-polio, yes, it occurs with aging and while we do not know exactly why some people have more weakness than others that are polio survivors, we do know that sarcopenia is a medical diagnosis that affects all of us as we age. It has an ICD 10 code. It is defined by World Health Organization. I'm pretty sure it plays a role. Sarcopenia means loss of muscle cells, and this occurs with aging in anyone neurologically intact individual, but in people with a neurologic deficit, you have three causes of sarcopenia. One is the neurological cause, just dropping motor neurons are going to kill muscle cells that are innervated by that motor neuron. That's the first.

[00:44:59] The other one is disuse. People with neurologic deficits will do less activity than the ones that don't. And we have disuse atrophy or sarcopenia. And then the other, the third one is aging. So, I think in between

those three and some genetic predisposition, I'm pretty sure that that plays a role why some adults with polio develop this post-polio syndrome, which is an exaggerated weakness in the areas that were previously affected by but not so bad by the neurologic deficit. So, yeah, it's another thing that we're studying, but we all know how to increase muscle mass. It's called exercise. And there are multiple ways of improving muscle mass and this is one of my pet peeves because it's such an objective outcome. You look at that muscle and you see it growing and we know how to do that. It's not -- this is not rocket science. So go back, we're going back to exercise, activity-specific exercise, targeted exercise that actually has the aim to increase muscle mass and that will prevent exaggerated weakness and in areas that have a neurologic deficit that relate to weakness.

[00:46:44] **Krissy Dilger:** Got it. Thank you. Okay. Our next question. Are there any supplements or special diet we should consider for my teen with AFM? Dr. Sadowsky, I don't know if you wanna address this.

[00:47:01] **Dr. Cristina Sadowsky:** Yeah, sure. I like to start. The best diet is the one that has a good balance in between protein about 40%, good fats 30% and good carbs 30%. And we all know what good carbs and good fats are. They're not the ones in chocolate and not the almond ice cream. Although you know a serving once a week is not bad. Specifically for muscle mass enhancement, obviously proteins play the best role. Supplements that have been studied and shown to improve muscle mass are creatine and I'm not going to go into the science of GMO or whatever that mold that you know, all of the people that are growing their muscles go to. But there are studies that are done in people with spinal cord injury in individuals with a lot of neurologic impairment, tetraplegia or so, that show that using seven to 20 grams of creatine per day if you really wanna do -- if you don't have a healthy diet and if you wanna add, you can do that. But I'm going to go healthy diet is the best.

[00:48:40] Supplements, if you live in an area in which you -- or you are lactose intolerant and you can take the calcium from and the vitamin D from natural sources then probably, but you should go and do it under a nutritional guidance but everything from a healthy natural diet is going to cover your needs at any time in your life. Do measure vitamin D and that's one of my pet peeves because we live in this very sheltered inside life in the United States and it's good to be like this because outside it's 110 degrees in some areas, plus too much sun exposure is not good for your skin. But I do think that measuring Vitamin D is something that you should do, but otherwise healthy diet.

[00:49:40] **Dr. Grace Gombolay:** I agree that's what I tell my patients and families. We don't have any specific data within AFM, but we do have data for example, in other inflammatory conditions like multiple sclerosis. AFM is not multiple sclerosis, I want to make that clear, but we know in other autoimmune conditions, healthy diets, olive oil, so the healthy fats of olive oil, more fiber, including more fruits and vegetables, we know that helps prevent inflammation and then trying to limit as much as possible. Like Dr. Sadowsky mentioned, especially your simple sugars or added sugars because that could potentially trigger inflammation in some people. So as much as possible avoiding that. Again, I think having a treat once in a while is not gonna be terrible for you. As much as possible, yeah more fruits and vegetables, protein, healthy diet, and I also check Vitamin D.

[00:50:31] **Krissy Dilger:** Great, thank you. Okay. Our next question came from a parent. Whenever my daughter is sick, she's out longer and it hits her harder than my other kids. Why does that happen? Is she immune compromised? Is her immune system affected for years after AFM? Dr. Gombolay if you wanna address this?

[00:50:53] **Dr. Grace Gombolay:** Yes. So, I hear this a lot in my patients with AFM and other related conditions. And when I think of immune compromise, I think of patients who are more, you know, immunodeficiency, meaning that they are more prone to infections. And like you're mentioning here, it takes longer to recover. But most patients who have that terrible immune deficiency, they're often being admitted because that's how

bad their infections are, that there's serious complications. I will say that patients who have that prolonged recovery from infections, it's hard to say where that's coming from. Is that related from inflammation because of it? Is it more related to fatigue? Because when you've had a neurological injury that increases fatigue when we see this across the board, whether you're a child or adult, you have any sort of injury in the past, even if you're doing well in good times when you have times of stress like an illness or infections, it can be harder to recover related to fatigue.

[00:51:57] And so it's hard when patients feel fatigued all the time. But we mentioned the good diet that's gonna be helpful, having regular exercise, there's actually data showing that exercise helps prevent fatigue and helps with fatigue, which sounds counterintuitive, right? Because if you're fatigued, you're not gonna want to exercise because you're getting more fatigue, but exercise actually helps with fatigue and then good rest and sleep. I will say it's one of those things, I didn't think I'd be talking a lot in my clinic about sleep, but I do it all of the time because we are all on our smartphones. Everyone has smartphones nowadays, even younger children, right? So, we're all on our smartphones. We're all watching things. We're on YouTube, we're on Instagram, we're on TikTok, we're on Facebook, we're on all of these social media things, which is great for connecting, but at the same time that affects our sleep. And so, there's a lot of people with poor sleep. So, we wanna make sure that we're optimizing those things so that way we can recover better from illnesses.

[00:52:58] **Krissy Dilger:** Got it. Dr. Sadowsky, did you wanna add anything?

[00:53:02] **Dr. Cristina Sadowsky:** No, no. Good diet, exercise, and sleep applied to everyone, lifelong. I think that's actually the answer for almost every kiddo.

[00:53:19] **Krissy Dilger:** Yeah, I agree. Okay. So, our next question is about treatment in that acute stage. So how is a new case of AFM treated? Does PLEX work best or if not, what does? Dr. Sadowsky?

[00:53:39] **Dr. Cristina Sadowsky:** I'm going to give that to Dr. Gombolay on that one because she does the acute care, I'm more in the acute. And I know there are three interventions that we use, but one is more favorable. But I'm going to let the specialist on that one.

[00:53:52] **Dr. Grace Gombolay:** Yes. So, if you're diagnosed with AFM, what we try to do and then we try to do these treatments early and what we do is we most -- there's no data showing that one treatment works better than the others, but most people will favor giving intravenous immunoglobulin or IVIG. The reason for that is that it can help if you have inflammation, it can help if in case you have an infection and then if somebody comes in with fevers and they're suspecting for AFM, we definitely want to make sure that there's not an active infection going on because other treatments like steroids, for example, could potentially make that worse.

[00:54:27] So definitely most experts will give and recommend IVIG. The other main acute treatments we will do in this stage can be steroids and can be plasma exchange or PLEX like you're mentioning. There's not a lot of good data supporting whether or not steroids or PLEX helps or hurts in AFM. So that's an ongoing conversation depending on severity of symptoms, depending on what the imaging looks like, how much white matter is involved, that sort of thing. What is the time course? Is the patient stable? And they're getting better or their symptoms getting worse? So, we have to do something right away while we're waiting for all those tests come back. So, it's sort of a case-by-case, a patient-by-patient discussion. But generally, I will give IVIG, and depending on what else is happening, we'll consider is definitely doing steroids or plasma exchange.

[00:55:24] **Krissy Dilger:** Great. Thank you. And this is kind of a related question. So, I'll just piggyback off of it. How long after an acute treatment is done? Do we know that it is or isn't working?

[00:55:35] **Dr. Grace Gombolay:** Yeah, that's hard because what we think in terms of IVIG is that even though we'd like it to work right away, and I have seen it work pretty immediately. Technically, peak effect of IVIG is 10 to 14 days, two to three weeks after we give it. So, it's one of those things where I generally wait three to five days after giving something before trying another treatment if I can. But again, if I give somebody IVIG and they're starting to get worse immediately, I'm not gonna wait those five days, I'm going to think about Okay, should we do plasma exchange? Should we do the steroids? Should we do something else right away? Because I don't want to wait for five days before giving it. So, it depends on what's happening and then if everything's stable, let's say somebody comes in with AFM, they're not in the intensive care unit, they're not in the ICU but they're not intubated. And we give the IVIG, but they haven't shown improvements, then we'll have that discussion and it's been five days and I'll have that discussion. Okay, what are some other treatments that we can talk about?

[00:56:42] **Krissy Dilger:** Gotcha. Thank you. Okay. Our next question is about a child going through puberty. So, how, if any, impact does AFM have on a child going through puberty? Dr. Sadowsky, I don't know if you wanna touch on this or if you want to pass it on.

[00:57:01] **Dr. Cristina Sadowsky:** Sure. No. I think that one of the things that I am looking for proactively is during the growth phase, there is this musculoskeletal component that is going to be affected by the fact that the child has paralysis. So, one of the things that I look for and I might have to address is scoliosis. And I do believe that there is a -- I know that there is a case series that looks at the neurologic level and the initial presentations and the likelihood of developing neurogenic scoliosis as time progresses. Another musculoskeletal complication that can occur in children that have not yet been walking is the formation -- is a hip dislocation, if the acetabulum, the little cup that houses the femoral head is not well developed because of lack of weight bearing in infants that have been affected by paralysis related to AFM before they were walking and weight bearing.

[00:58:22] Other things, if there are-- again musculoskeletal that might be limb length discrepancy that we need to address. Bone mass is supposed to increase, and we all know that children with neurologic dysfunction, including children with AFM will have conditions that will have a decreased bone mass, especially in the limbs affected by paralysis. So, looking proactively to avoid fractures and those kinds of injuries, that's kind of -- Oh, maybe I would add children that are vent dependent before the age of eight so early, they might actually improve because the thoracic cavity grows and becomes more stable starting at the age of eight or so. They might be able to get off the ventilator for periods of time or forever. I'm trying to think. I don't know. Right now, no hormonal problems that I am aware of. So, if that was the intent of the question, I am -- there are no reported hormonal consequences of AFM. So mostly musculoskeletal from what I can say.

[00:59:57] **Krissy Dilger:** Got it. Dr. Gombolay, anything to add really quick before we can [crosstalk]

[01:00:01] **Dr. Grace Gombolay:** No, I don't. Yeah, I agree with what Dr. Sadowsky said. So, yeah.

[01:00:05] **Krissy Dilger:** Okay. Awesome. Well, thank you both so much. Unfortunately, this hour flew by because you guys did such an amazing job at answering all these questions, but we are out of time at this point. But just thank you both so much and hopefully, we can continue this conversation in the future and maybe answer a few more questions. Thank you. Have a great rest of your day.