

Speaker 1: This podcast is for informational and educational purposes only and is not to be considered medical advice for any particular patient. Clinicians must rely on their own informed clinical judgments when making recommendations for their patients. Patients in need of medical advice should consult their personal healthcare provider.

Carolyn Coyne: [I'm Carolyn Coyne.](#) I'm a scientist in the Division of Pediatric Infectious Diseases.

Brian Martin: [I'm Brian Martin](#) , Vice President of Medical Affairs here at UPMC Children's Hospital of Pittsburgh. Today we're fortunate to bring you a special edition of That's Pediatrics, featuring [Dr. John Williams](#), Division Chief of Pediatric Infectious Disease here at Children's. Our topic is [acute flaccid myelitis](#), a condition that's been top of mind for many parents, clinicians, and families in our region and nationwide. This topic has been highlighted in both the popular media and social media.

Today, in conjunction with Dr. Williams we look to bring you up-to-date information regarding the diagnosis and prevention of acute flaccid myelitis, its association with certain viruses, and also how we're interfacing with the Centers for Disease Control to assess the situation here in Western Pennsylvania.

Welcome, Dr. Williams.

Dr. Williams: Thanks, Brian. Thanks, Carolyn. Good to be here. I'm normally here as a host, as regular listeners may know. It's a pleasure to be a guest.

Carolyn Coyne: Tables have turned.

Dr. Williams: Do I get two checks for this?

Carolyn Coyne: I think, yes. It's in the mail.

Brian Martin: Yes, yeah. Yeah, yeah.

Dr. Williams: Oh wait. That's right. We don't get paid for this.

Brian Martin: Thanks for reminding us.

Carolyn Coyne: John, maybe how we could start this is just to give a little background to the listeners as to what we're seeing with these cases. Are they unusual? On your side, of course, as being the division chief of Peds ID, when you first became aware of this and where we're at now?

Dr. Williams: Sure. Acute flaccid myelitis or AFM, as I'm going to call it through most of the podcast, is an acute neurologic disorder of childhood that usually has an onset over a couple of days, and it presents as weakness usually of arms and legs. It's often asymmetric or uneven. So it's often one side is affected more than the

other. That is really clinically how it presents. Children can have other symptoms such as fever or respiratory or intestinal, but without that weakness of the arms and legs it's not AFM. That's really the key feature that the child will have.

AFM has been known and occurs sporadically for a long time. In fact, we may touch on this later, but 60 years ago before the polio vaccine, there were tens of thousands of cases of severe AFM or paralytic polio myelitis every year in this country. Since then, there are some cases but not that many. Starting about four years ago in 2014, there was a large national outbreak and there were about 150 cases. Again, in 2016, there were about 150 cases. 2015, 2017, there were only a couple, a few dozen. This year so far, there look to be a lot of cases as well. It's been noticed nationally over about the last month or so in many places in the country that people are seeing a lot more cases like we did in 2016, like we did in 2014.

Brian Martin: John, can you speak to outside the United States? Are you aware with your infectious disease colleagues of speaking about the impact of AFM globally?

Dr. Williams: Yeah. AFM globally, until very recently, the last, say, 10 to 15 years the major cause of AFM globally was polio. Anybody under the age of 55 has forgotten it in this country, but it was still a major cause of severe AFM and paralysis worldwide. Polio now, due to vaccine, is down to only a couple of countries. So it's on its way to being eradicated. The other viruses that can be associated with AFM are found in other countries in the world. Although in every country in the world, it's pretty rare in childhood.

Carolyn Coyne: Well, then just to clarify that. You sort of immediately draw our attention to viruses. So I'm curious as an ID doctor, a parent maybe brings a child into the clinic or into the emergency room with AFM. What do you suspect initially is the causative agent, and then what is your plan to diagnose it and to treat it? What are the options?

Dr. Williams: That's a great question. Most cases of AFM that have been studied, and it's only been more closely studied in these large outbreaks in 2014 and 2016 and now 2018. Most cases, a specific cause is not found. But of the causes that are found, most of them are viruses. There's a number of different viruses that we'll probably talk about. What we do is first ask the family any exposure the child may have had or any recent illnesses. In terms of caring for the child, we don't have medicines for most of these viruses. So the treatments we provide children who come to the hospital with AFM are supportive care if they're having problems with breathing or blood pressure or circulation or things like that.

If we think they have a lot of inflammation, if their immune system is very activated, they might be treated with medicines to affect their immune system. And then we do a lot of testing. We do blood testing to look for different infections. We do spinal fluid testing to look for different infections. A key part of it is an MRI, which is a special imaging technique of the brain that can reveal

patterns that can really tell you if the child has AFM or some other kind of nerve disorder.

Carolyn Coyne: We've been talking a lot about, obviously, children. Here we are at CHP, but could you talk maybe a little bit about AFM in terms of who's afflicted by it? Certainly we know that a lot of young children seem to be more sensitive and why is that? At what age are children at greatest risk for this?

Dr. Williams: We know that about 90% of cases of AFM occur in people under the age of 18, so most of the disease is in children. The mean age is about five to seven years old, so it's mainly younger children. Why that is we don't really know. We think that viruses are a common cause of AFM, and there are literally hundreds of different viruses, common viruses, that children encounter during the course of childhood. All of us encounter these viruses as a natural part of growing up and building a healthy immune system. So it may be that children are encountering some of these viruses for the first time.

There's also thought that it might have something to do with the fact that children's immune systems may not be as fully developed as an adult. But the truth is, we really don't know. There's much more we don't know about AFM than what we do know.

Brian Martin: John, could you speak a little bit about other aspects of the differential diagnosis? We have pediatricians and families that could be listening to the podcast here. We've sort of honed in on viruses, but what other things do you see that might present something like this that could worry a pediatrician or a family that this could be a case of AFM? I really liked how at the beginning you were very specific about that unilateral weakness being kind of a hallmark of this to allow the clinician to make a really informed decision at the beginning of the differential. But are there other things that look like this that clinicians could be thinking about?

Dr. Williams: Yeah. I think that's a good point, Brian. That is a key thing is the weakness because we've been talking about viruses and how common viruses are. Any of us who have children or work in a children's hospital like this know how commonly kids get runny noses and coughs and vomiting and diarrhea and rashes. None of those things are AFM, so it really is the thing is for the parents and the care provider to notice that there's weakness of one or more arms and legs. And then in addition to AFM, which is a distinct kind of disease that causes weakness, there are other diseases such as there some immune diseases where the immune system actually attacks the central nervous system.

One of those that people have heard of perhaps in adults is called multiple sclerosis. We rarely see that in children, but there are similar kinds of diseases where there's no infection, but the immune system is attacking the nerves. We would treat those differently than we might treat an infection. We don't see this much in this country because we have clean water and a clean environment. Yes, even here in Pittsburgh, former steel town, we have a very clean river. But

certain toxins or heavy metals can also cause a similar kind of weakness or paralysis.

Carolyn Coyne: Maybe now we can transition to talking about the possible viral suspects. Of course, you mentioned that a child comes in, you would run a panel of tests to confirm that it's AFM. Now you want to figure out what it is. Maybe you could talk about the most likely suspects and how you go about that diagnosis, and maybe we could talk a little bit more about what it means, what those suspects do.

Dr. Williams: The major viruses we think of, and then I get to play host in a minute here. One is a group of viruses called enteroviruses. Much less commonly in children in most years and certainly in this year is a virus that's transmitted by mosquitoes called West Nile virus. I would just note that the CDC said in the last day or two that of the current cases that they are studying this year, none of them are due to West Nile virus, but West Nile virus can cause an asymmetric paralysis. We really don't see it in this country, so unless somebody has traveled it wouldn't be relevant. But there's a virus called Japanese encephalitis virus that can cause this.

Polio, which I just mentioned, is now, thanks to the polio vaccine, only circulating in a couple of countries in the world, the major two being Pakistan and Afghanistan and Nigeria. And then rabies virus, which is extraordinarily rare in humans. When a virus is found, the most common virus that's found is an enterovirus. Carolyn, I happen to know since our labs are close to each other, that you are a leading expert in enteroviruses. So maybe you could tell us about enteroviruses.

Carolyn Coyne: Sure. Yeah. My lab has been studying enteroviruses for about 15 years now. I started actually doing this when I was a postdoctoral fellow. I can tell you a little bit about enteroviruses, maybe even the things that we do, but how it relates to this. Enteroviruses are a very, very common cause of human infection. In fact, they are listed by the CDC as the most common infectious viral agent of humans. That's largely because it's a large family of viruses. As the name would suggest, and I always like to remind people that you can impress your friends by the names of viruses and how you can figure out what they are because an enterovirus is an enteric virus, as the name would suggest.

These viruses are most commonly transmitted by what we refer to as the fecal-oral route. So viruses of an infected individual are shed at usually very high levels in the feces. Of course, you then become exposed to the virus during initial transmission by potentially touching a contaminated surface with feces, putting it to your mouth of course, eating, ingesting any food or certainly water that's contaminated with that feces, and that's really the most common route of transmission. With some of the viruses, they can actually also be transmitted by the respiratory route. Much like we think about flu, let's say, these viruses can also enter through our upper respiratory tracts as well.

It's a very, very large family of viruses. There are over 100 serotypes of these viruses. You mentioned before polio virus. I think certainly that's the most widely-known within the family. But what we know is there's a lot of other members of the enterovirus family that cause severe disease primarily in children. If you really look at the spread of the disease manifestations and the severity of disease, mortality, morbidity, we certainly see this in children below the age of one or two the most. And then there's another peak of complications in the elderly, which as you referred to before, is really likely driven by the immune system at both of those stages of life.

But there are over 100 different serotypes of enteroviruses, so we know polio types. But some of the other more common ones that we think about are Coxsackieviruses. This includes Coxsackievirus A or CVA. For any parents of children in daycare or perhaps in elementary school, you probably know this virus and hate this virus because it's really one of the more common causative agents of hand-foot-and-mouth disease. Children, you can often see signs, I see them all the time in my son's daycare when I pick him up, of Coxsackievirus. Usually how that virus presents is, at the name would describe, you get blisters and sores on your hands, your feet, and in your mouth.

There's other viruses in addition to Coxsackieviruses. There's enterovirus 71, EV71. This is a virus that much like, I think, some of the other enteroviruses have been associated with really widespread global outbreaks. In fact, in China there was an outbreak between I think it was 2007 to 2012 where there were over seven million cases of infection. For that virus, it's also associated with hand-foot-and-mouth disease, but this is a virus that's also commonly associated with AFM. So oftentimes the more common kind of symptoms are hand-foot-and-mouth, it's also associated with acute flaccid paralysis.

In addition to that, there's lots of other viruses that are not as perhaps well-known, and those include ECHO viruses, also that impact the young, as well as another, I would say, more emerging enterovirus, which is called enterovirus D68 or EV-D68. This is a virus that has really been associated with a lot of the AFM cases certainly within the United States during these kind of peak outbreaks that you mentioned, 2016. EV-D68 is a little bit unlike some of the other enteroviruses just in the route of transmission. I mentioned before that enteroviruses are primarily transmitted by the fecal-oral route. For EV-D68, it's a little bit of an anomaly because it really seems to prefer, if you will, a transmission through the respiratory route.

So it resembles a little bit more of what we think of as a rhinovirus or the common cold virus, which actually is also officially within the enterovirus family. EV-D68 though is also associated with very high rates of AFM and has been, I would say, one of the common causes of these more recent outbreaks certainly within the United States.

Dr. Williams:

I think then, I mean that leads me to one point that you just touched on is about the fact that these viruses are spread either by the fecal-oral route or by the

respiratory route. So in terms of prevention of infection, the classic recommendations that our mothers all hopefully taught us which is to cough and sneeze into your elbow and then hand hygiene with hand gel or soap and water.

Carolyn Coyne: The other thing that I would just note too is that these are very, very common viruses. We have all had these viruses many times in our lives. Kids get these viruses every year. It's actually a very, very rare outcome of these viruses to develop AFM. I mean, this was the same for polio virus as well. Many cases of infection with these viruses are completely asymptomatic within children, within adults. You never know you've been infected. Certainly the most common is just what you would think of as a mild cold or flu-like symptoms. You would have a fever. You certainly wouldn't feel well. So it's a very, very actually rare complication to have AFM.

Although these viruses are widespread and certainly exposure is quite common, it certainly really should be noted that most individuals and most children infected with these viruses will not go on to develop AFM.

Brian Martin: As the non-virologist, non-infectious disease specialist in the room, I did a little back of the napkin math to give our ... our viewers, my goodness, our listeners-

Carolyn Coyne: Good thing they're not viewers.

Brian Martin: Yeah. Good thing. Good thing, yes. I have a face for radio. But to give our listeners a little bit of perspective on that, in 2016 the census said there was approximately 74 million children in the United States and we're talking approximately 150 out of ... And those are children under 18, so 150 cases out of 74 million gives us a little bit of perspective. I actually did the math, so in terms of it's a .0002% incidence. It's a very rare event. I think that one of the takeaways for me as a parent and as somebody that obviously has a lot of people asking me questions about this, is that the vast majority, from what I'm hearing from you, is the vast majority of enterovirus infection is self-limiting.

It's a hand-foot-and-mouth presentation where a child will have some fever, might have a little bit of dysphagia for a time, not feel well, but will have a full and complete recovery and that the basics, John, to your point, about prevention here really revolves around the basics of what we would do for a cold or a flu, which is essentially perform good hand hygiene and mind your sneezes and other things that we do to help prevent respiratory illness.

Carolyn Coyne: Yeah, absolutely. Maybe what we could end on, and I'll throw this back to John so we can put our hats back on where they were to begin with. Maybe just to finish up, you could provide advice for parents who might be worried. Again, I'm the parent of a young son and so I can appreciate this. Just to let people know what symptoms to look for, and then when to potentially think there is cause for concern.

Dr. Williams:

My kids are older now, but I get no less concerned about them than I did when they were young. It is scary for parents when you hear about things like that. So I think first we have to remember that this is very rare, as you just said, Brian. It's less than one in a million. Before polio vaccine, there were over 15,000 cases of paralysis a year in this country, before the polio vaccine, invented by Jonas Salk here at University of Pittsburgh. So yay vaccines. Thank you.

The viruses are very common, as you said. So in terms of prevention, really it's hand hygiene but letting kids be kids. They should still be going to daycare and going to school because most of those million kids who get any of these viruses are not going to have AFM. I think in terms of watching their children, it's really watching for the sign of weakness, a child who's not using one of their arms to feed themselves the way they should or not walking well or something like that. If they just have respiratory symptoms or vomiting or diarrhea, that shouldn't make the parent concerned that that child is going to have AFM.

One final point, because I think as parents and pediatricians we all think about protecting our own kids and protecting other kids. Everybody is appropriately concerned about a potentially very serious disease like AFM, of which we said there were 150 cases in these peak years. Okay, so influenza, there are tens of thousands of children hospitalized every year in the US and several hundred children die of flu in the US. Almost all of those are unvaccinated. So in addition to what we talked about, I think the most important thing any parent or care provider can do for their children is to get a flu shot, and it's time right now.

Carolyn Coyne:

Yes.

Brian Martin:

That is a fantastic point, John, and I think a great thing to close on.

Carolyn Coyne:

Thank you so much for joining us, John.

Brian Martin:

Thanks very much for your time.