An Update on Poliomyelitis

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Dr. GG deFiebre: [00:00] Hi everyone and welcome to the SRNA's “Ask the Expert” podcast series. This podcast is titled “An Update on Poliomyelitis.” My name is GG deFiebre and I moderated this podcast. 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. Our “Ask the Expert” podcast series is sponsored in part by Horizon Therapeutics, Alexion AstraZeneca Rare Disease, and Genentech.

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[01:27] For this podcast, I was pleased to be joined by Dr. Sarah Hopkins, Dr. Katie Lockwood, and Dr. Amy Rosenfeld. Dr. Sarah Hopkins is Section Head of Multiple Sclerosis and Neuroinflammatory Disorders at Children's Hospital of Philadelphia. She has an interest in inflammatory disorders of the spinal cord and directs the multidisciplinary Myelitis Clinic at CHOP. She has an interest in acute flaccid myelitis or AFM and serves as a neurology consultant for the US Centers for Disease Control and Prevention, or CDC, for activities related to AFM surveillance. She is the site PI for the NIH AFM natural history study and the international pediatric opsoclonus-myoclonus-ataxia syndrome registry. Dr. Hopkins serves as codirector of the CHOP-PENN Age-Span MS and neuroinflammatory disorders fellowship.

[02:17] Dr. Katie Lockwood is a primary care pediatrician at Children's Hospital of Philadelphia. She's the Director of Education for the CHOP Primary Care network and the host of “Primary Care Perspectives” podcast. Dr. Amy Rosenfeld received her PhD training in virology in the laboratory of Dr. Vincent Racaniello at Columbia University. After her postdoctoral fellowship at McGill University, she returned to the Racaniello lab where she focused her research on elucidating the mechanisms by which infection with enteroviruses leads to acute flaccid myelitis. In the spring of 2022, she established her own laboratory within the Division

of Viral Products at the Center for Biologics Evaluation and Review at the Food and Drug Administration, where she continues to study the mechanisms by which enterovirus infection can lead to the development of acute flaccid myelitis.

[03:05] Thank you for joining me today. Today, our podcast is going to focus on poliovirus and poliomyelitis, the neurological disorder that results from the virus infection. Poliomyelitis presents as acute flaccid paralysis. Both the endemic virus, poliovirus, and the disease poliomyelitis are thought to be eradicated in the United States. However, a virus and disease are still circulating worldwide. The absence of global eradication allows for the reintroduction of this virus and disease into areas where the virus has been declared as eradicated. This recent event that we've all heard about in the news, the reintroduction of paralytic poliomyelitis in the United States, occurred recently in the New York City area. And this was a young man who was diagnosed with paralytic poliomyelitis. He was unvaccinated but the virus isolated was genetically identified as a variant of the Sabin type two poliovirus, a component of the oral poliovirus vaccine. This vaccine, OPV, is an acronym, or oral poliovirus, is no longer administered to children in the United States but it is still used in many countries including those in South America and Asia.

[04:17] This particular case is significant because it really demonstrates the importance of and the need for unified global health policy and how travel can really facilitate the movement of poliovirus and poliomyelitis around the world. And so, we do have two very effective vaccines against poliovirus and poliomyelitis. The news of this case report is obviously a concern to members of the SRNA community as well as the general public and really a reminder of a devastating disease that was once an epidemic in the United States. So today, we have experts here in poliomyelitis who will answer questions and concerns that those in the SRNA community might have. Just going to briefly introduce everyone. We have Dr. Amy Rosenfeld, who is a virologist formerly at Columbia University and now a principal investigator at FDA. We also have Dr. Sarah Hopkins. She's a pediatric neurologist at Children's Hospital of Philadelphia. And then Dr. Katie Lockwood also is a pediatrician at Children's Hospital of Philadelphia. So, thank you so much for joining us today to talk about this. So first, Dr. Rosenfeld, do you mind just telling us about poliovirus as an infectious disorder? How is virus infection acquired and what type of virus is poliovirus?

Dr. Amy Rosenfeld: [05:35] Thanks for inviting me, GG. Poliovirus is a small single-stranded RNA virus that's related to another virus that we think of when we think of acute flaccid myelitis, or AFM, and EV-D68 or EV-A71. Unlike EV-D68 but more similar to 71, this virus is orally typically transmitted. So, it's really important to have sanitary conditions because the water supply is where the virus is found and how it can move from person to person. So, you want to make sure that we have really clean water, and it actually was known as a disease that was a sanitation disease because when it was first isolated, you saw it in children that were very young. But as the United States developed a sanitation system, it moved to children that were slightly older when the maternal antibodies and protection had waned or had not been replaced by exposure.

Dr. GG deFiebre: [06:49] We hear people refer to polio but what do people mean when they say that? And also, how does poliovirus cause poliomyelitis?

Dr. Amy Rosenfeld: [07:01] When we colloquially talk about polio, we're talking about both the virus and the disease poliomyelitis. And when we talk about poliomyelitis, we're colloquially talking about paralytic poliomyelitis because anybody who gets infected where the virus can replicate has poliomyelitis. It just does not cause paralysis in the majority of cases. So, 1%, one out of every 100, one out of every 1,000 actually develops paralytic disease. But everybody is infected and sheds infectious virus. So, we have to be very careful about what we're talking about whether or not we're talking about poliovirus or paralytic poliomyelitis. And so, the

way the virus causes disease is we ingest it, and it replicates within our alimentary tract, our small intestine. And then in some cases, it enters the bloodstream and then traffics into the central nervous system and can infect the neuron. And those neurons are generally the neurons that innervate our lower limbs, so you see below the waist paralysis in the majority of cases. There are times when it can actually enter the brain and it will be called bulbar paralytic poliomyelitis. And that is even more infrequent than paralytic poliomyelitis.

Dr. GG deFiebre: [08:37] Thank you for that overview. Dr. Hopkins, how does poliomyelitis present in a patient? What are the major symptoms parents or health care providers should really recognize as concerning symptoms of poliomyelitis?

Dr. Sarah Hopkins: [08:53] In order to understand a little bit about the symptoms that occur, I want to expand a little bit on what Dr. Rosenfeld mentioned about the nerve cells that are affected. In your brain and spinal cord, you've got two major nerve cells. You've got the first one that goes from your brain to your spinal cord and that one connects with the second one, which is called the anterior horn cell or the motor neuron, which is in the anterior horns of the spinal cord. And then that goes out to supply the muscles in your arms and legs. So, it's that second neuron that is affected in paralytic poliomyelitis and because that's the nerve that's affected, patients get what we call a lower motor neuron presentation. And what that means is that the involved extremity gets floppy and very, very weak. The presentation often starts with potentially even some pain in the affected limb. As Dr. Rosenfeld mentioned, they can have some weakness in their muscles for swallowing and things like that. And in paralytic poliomyelitis most often it was the lower extremities affected. Tends to be the muscles that are closest to the body, so what we call proximal muscles more than distal muscles. So, things for families to watch for are really the onset of some weakness of extremities or the muscles of swallowing in the setting of a current or recent febrile illness.

Dr. GG deFiebre: [10:47] Thank you for that as well. Dr. Lockwood, poliovirus is an infection that is preventable with vaccination. Do you mind just telling us in a little bit more detail what happened with the recent report of poliomyelitis in New York? And what do families and parents need to know about prevention of infection and poliomyelitis through vaccination?

Dr. Katie Lockwood: [11:09] Thanks for having me. I'm a primary care pediatrician and the inactivated polio vaccine, or IPV, is part of the repertoire of what we call routine childhood immunization. So, it's an immunization that we give to all children as part of the vaccines that they get before going away to school. It's a recommended vaccine for school attendance that involves four different shots at the ages of two months, four months, and the third dose being between six and 18 months, and then the fourth dose between four and six years old. What happens and what we think happened in New York is that there are sometimes people who refuse routine immunizations for a variety of reasons. Some communities have higher rates of vaccine refusals, so we can have communities that are particularly vulnerable when there is virus present in the community. You need to have a certain number of people in your community vaccinated for what we call herd immunity. And for polio, the World Health Organization estimates they need about 80% of your community vaccinated to have protection against polio spreading within your community.

[12:26] And so in the case in New York, in Rockland County, when you look at kids under two, now the person who had the case there was a 20year-old, but when you look at vaccination rates for the community in the population who's normally being vaccinated for polio, only about 60.5% are vaccinated for polio. And you compare that to the New York State average of 79.1%, both are below herd immunity. Certainly though New York State is closer than that county. And so, we worry about communities with low vaccination rates being at risk for these vaccine-preventable diseases. And as you mentioned, the key here is that this is preventable.

And so, getting routine childhood immunizations can help offer protection for people who are worried that they may be exposed or at risk due to cases in their community.

Dr. GG deFiebre: [13:17] Have we seen any changes in vaccination rates during the COVID-19 pandemic?

Dr. Katie Lockwood: [13:24] Definitely early on in the pandemic. In the first four months of the pandemic in 2020, vaccination rates globally dropped. It's estimated that about 23 million children missed their vaccines in 2020 and about 17 million of those kids had no vaccines during that time period. There has been significant catch-up though because initially during the pandemic we were encouraging families to stay home, to not go to the doctor's office unless they were ill and needed care. And so many families skipped routine immunizations at our request to not overwhelm the healthcare system during those early months. But then we made swift efforts to catch up vaccinations. And the kids under two who come in to see their pediatrician more routinely and regularly every few months, usually in those first two years of life, they were able to catch up much more quickly than some of the older children.

[14:21] And so the groups that we worry about still having delays from the pandemic are some of the older kids who only come annually. In that series of vaccines that I talked about for IPV, the fourth dose is between four and six years old. So, there may be some kids in that age group who didn't get their fourth dose because they skipped their annual and now maybe they're a year or two behind in their vaccines. We do know that there's many kids who suffered delays in their vaccinations due to the pandemic as well as we know that during 2020, the Global Polio Eradication Initiative was put on delay for four months. So, there's a global delay and countries that have less infrastructure in catching up are behind other countries. And so, we do see some disparities globally as well as locally in terms of resources.

Dr. GG deFiebre: [15:16] To go into a little bit more detail about the vaccines, Dr. Rosenfeld, do you mind talking about the vaccine, why there are two options for vaccination around the world?

Dr. Amy Rosenfeld: [15:27] There are two options because of the way there was kind of a race to develop the vaccine. There had actually been, in the 1920s and early 30s, attempts to make vaccines against poliovirus infection and the development of paralytic poliomyelitis. And out of those studies, one predominant scientist came to the forefront and that was Jonas Salk. Jonas Salk was a flu virologist and he had been inactivating influenza to make a vaccine. And he applied his technique or methodology to poliovirus, and he was able to demonstrate that if you inactivate poliovirus and you administer it to animals and then you challenge them, you're able to protect them from the development of paralytic disease. And subsequently his vaccine was initially licensed in the United States in 1955.

[16:35] At the same time during the 1950s, Albert Sabin, who was a pediatrician, came to the conclusion that that vaccine didn't confer the appropriate immunity that was required in order to protect against any infection. This is a little bit of where Albert was a little bit hasty in the fact that vaccines don't protect against infection, they protect against the development of severe disease. But he still pursued this, and he came up with infectious attenuated strains of the three stereotypes of polio, which is what OPD is, and we refer to it as oral because it's administered in the mechanism by the way natural infection occurs. So, you orally ingest the vaccine, and you orally ingest polio. And subsequently actually the United States did not license his vaccine when he applied. They said, "We have a vaccine; we don't need yours." And so, he actually tested and did a lot of work, and it was first actually licensed in Russia before it was licensed here in the United States. There was an episode in which IPV, or the inactivated vaccine was not properly manufactured and then the United States came back and said, Albert, we really want your vaccine. And so, it is the vaccine that has been administered in this country until 2000. And it has really led the effort to protect all of us against the development of paralytic poliomyelitis.

Dr. GG deFiebre: [18:22] Should parents in the United States be concerned about the reemergence of poliovirus and poliomyelitis has been noted in some other countries?

Dr. Amy Rosenfeld: [18:31] Concerned in what respect?

Dr. GG deFiebre: [18:33] That it might re-emerge in greater numbers than this one case that we're seeing at the moment.

Dr. Amy Rosenfeld: [18:39] Well, poliovirus has always been circulating in the United States. One of the reasons why we don't see it here is because of the vaccine coverage in the public. As Dr. Lockwood talk said, throughout the country, it has been 80% or greater and so we don't see it. Once that dropped, we see it. What actually this case demonstrates is the importance of vaccination, not the opposite. It demonstrates the importance of a coordinated global health policy in continuing to vaccinate our children to protect them against the development of paralytic poliomyelitis. So, it's not just that this population should be concerned any more than any other parents should be concerned. It should be that we need to reinforce the need to be vaccinated and the importance of the vaccines.

Dr. Katie Lockwood: [19:46] And I would add to that that if you are vaccinated, you shouldn't be worried about getting polio. The fact that inactivated polio vaccine that we give in the United States works very well at preventing polio infection and so there's no need to worry if you are vaccinated.

Dr. Amy Rosenfeld: [20:03] Right. But it prevents the development of paralytic polio, it does not prevent infection. And what it is and what allows us to think about it being eradicable is the fact that the durability of immunity elicited by the vaccine is so very, very long. In order to eradicate anything, you have to have a durability of immune response for your life. So, your child or you who got vaccinated and haven't gotten vaccinated since five are protected from the development of paralytic poliomyelitis.

Dr. Katie Lockwood: [20:47] Because there haven't been cases that we've seen in such a long time, this vaccine is somewhat a victim to its own success in that some communities think that the vaccine is not very important because they haven't seen people with polio in their lifetime. And so, there are many people who are making decisions about which vaccines to give their child. And I hear this in clinic all the time as I'm sure you do as well that they only want to give the vaccines that are most important or they'll say, which infection is my child most likely to get? And I think many of us would agree that for a while until very recently, polio would be low on that list if I were ranking among the vaccine-preventable diseases which one their child might be at risk for. But we are global citizens, and we know, as Dr. Rosenfeld just pointed out, that this is not eradicated globally. And so, it's still important, even though you're not seeing polio every day in your community, it's still important to get vaccinated because there is risk out there, especially in communities, again, where vaccination rates are low.

Dr. Amy Rosenfeld: [21:57] Well, I think that this demonstrates the importance of vaccination and I think what it says is actually the opposite. It says that this vaccine is super important because many people have forgotten the devastation of the outbreaks of poliomyelitis that occurred in the 1920s, 30s, 40s, 50s where children were not able to go swimming, they were not able to go play outside. And mom's retorted to their child when they wanted to do these things, what, are you crazy? You want to spend your life in an iron lung? So, it actually demonstrates the importance of this vaccine. It also demonstrates how careful you need to be when you declare something eradicated that is basically silent in 99% of the people. So, one of the caveats of polio infection, poliovirus infection, is that you don't really develop symptoms. You might get a fever. You might have a little flu like symptom but that goes away in about 24 to 72 hours after you're initially infected and you don't even know. That is one of the things about this case is that it came from a traveler who was

somewhere in a country that is getting and using and administrating OPV and he either received a dose of OPV or was exposed to somebody who had a dose of OPV and got infected. He didn't develop any symptoms; he was perfectly fine, and he got on a plane, and he trafficked it or transported it here to the United States. And he still doesn't have any symptoms. Everybody else that he saw was exposed and they didn't develop any symptoms except for one person. Unfortunately, that one person's genetics is what defined whether or not he was going to develop paralytic disease or not.

Dr. GG deFiebre: [24:26] In the SRNA community too we've heard about acute flaccid myelitis and have families with children and adults with acute flaccid myelitis. So how does poliomyelitis differ from acute flaccid myelitis or AFM? Dr. Hopkins?

Dr. Sarah Hopkins: [24:44] Like we talked about a few minutes ago, poliomyelitis is an infection that affects the anterior horn cells of the spinal cord and AFM is also an infection that affects the anterior horn cell of the spinal cord. The virus is different. We think that the virus associated with acute flaccid myelitis is predominantly enterovirus D68 and some other viruses likely cause the presentation as well. Similar to paralytic poliomyelitis, when patients present with AFM, they present with the acute onset of lower motor neuron weakness, so weakness where that extremity is floppy, where we have decreased reflexes in that extremity. Again, it's usually in the setting of a current or recent febrile illness. Often those kids have upper respiratory infections when we're talking about AFM and also pain in the affected extremity. It's usually asymmetric - one extremity is affected more than the others. And usually, again, as with polio, more of a proximal over distal weakness. So often the hands are working fine, the feet are working better, but kids are unable to lift their hands over their head or squat down and stand back up, things like that.

Dr. GG deFiebre: [26:14] What about the difference between poliomyelitis and something like transverse myelitis as well?

Dr. Sarah Hopkins: [26:20] The presentation there can actually be significantly different. There are less similarities with transverse myelitis than there are with AFM and poliomyelitis. So, when we talk about transverse myelitis, we're typically talking about an autoimmune or a post-infectious syndrome where most of the damage is really being done by the immune system and not by a viral infection itself. For that reason, in transverse myelitis, while you can have the anterior horns of the spinal cord infected or affected rather, the injuries typically much more involve the white matter of the spinal cord. So instead of getting that second nerve affected, you get the first one more affected and that causes what we call upper motor neuron problems where the extremities get weak, but they also get really tight, and you have increased reflexes in those extremities. You're also with transverse myelitis much more likely to have sensory trouble, so trouble with the way your body feels temperature and touch and vibration, things like that. That also does impact sometimes the treatments that we choose for those disorders as well.

Dr. GG deFiebre: [27:50] Some of those with rare neuroimmune disorders like ADEM, MOG antibody disease, neuromyelitis optica spectrum disorder, transverse myelitis, or AFM as well may not have been vaccinated against poliovirus. What is the general recommendation for children or adults with these disorders and these vaccines? And then, what about those on immunosuppressants as well?

Dr. Sarah Hopkins: [28:15] I think the general recommendation is very, very clear. If you have a known disorder that puts some areas of your spinal cord at risk or that puts you at risk for a spinal cord disease, then you absolutely don't want to put yourself at risk for another spinal cord disorder that puts your function at risk as well. So, we absolutely recommend that our patients with these neuroimmune disorders be vaccinated for polio. And when we think about patients on immunosuppression, we typically do recommend that our

patients that are on immunosuppression be vaccinated. Most often, we like to vaccinate them before they're immunosuppressed so we can ensure an adequate response to the vaccine.

[29:09] But taking our most common therapies, which are typically anti-CD20 medicines, like rituximab, we know that patients do still mount a response even when they're immunosuppressed. We typically do try to avoid live vaccines in those patients, but the IPV vaccine is not a live vaccine and it's safe for those patients. It is very important for patients and families to talk to the provider that's prescribing the medicine because there may be some timing issues that might be you might get a slightly better response if you give it at one time over another. But most of us would still recommend -- not most of us, really all of us would still recommend that those patients be vaccinated with IPV vaccine. It's just a matter of timing and discussing it with your provider.

Dr. GG deFiebre: [30:13] Now we've talked a bit about poliomyelitis and its implications, what is needed to be done by public health agencies, healthcare providers, like pediatricians, neurologists, infectious disease specialists, family physicians as well as parents and families? Dr. Lockwood, do you want to answer first?

Dr. Katie Lockwood: [30:32] I can start from the outpatient perspective. So certainly, pediatricians can ensure that their patients are up to date with routine immunizations including IPV. And we can also ask parents who may not be up to date if their child didn't get a vaccine, we can check to make sure that they've had that vaccine because adults can do catch-up immunizations for polio as well. And if families are traveling to any high-risk countries, there is an accelerated vaccine schedule that can be done to ensure that they try to get as many doses as possible prior to their travel. And so, I think education and answering questions that families may have, if they have any hesitancy about vaccines is something that primary care pediatricians do all the time. We're happy to have those conversations with families who may be seeing things in the news about polio and have questions about which vaccine their child received and what they should get moving forward. And so, we are happy to have those conversations and answer questions from families.

Dr. GG deFiebre: [31:39] And then Dr. Hopkins?

Dr. Sarah Hopkins: [31:42] I think the first thing, as a neurologist, the first thing that this changes is really just the awareness and needing to be more cognizant about considering polio in our patients who present with acute flaccid myelitis. We have always been careful to ask and be sure our patients were vaccinated but I think this recent case just underscores the need to do that. I think the other thing that health care providers need to continue to do and be very careful about doing is just checking in with all our families on a regular basis because this does, I think, underscore the need to make sure all of our families are protected even when we maybe are not seeing them for a routine well-child check or it's not a situation where we normally go into a detailed discussion about vaccinations.

Dr. GG deFiebre: [32:39] And then Dr. Rosenfeld, what about in terms of surveillance or public health agencies?

Dr. Amy Rosenfeld: [32:47] We have always advocated for wastewater surveillance here in the United States. And now the CDC has come out, the Chief of the polio lab has come out and said that there should be environmental surveillance in areas such as New York, London, and Jerusalem of high travel. But I know that many states are on board with doing wastewater surveillance and then knowing that it's here and really aggressively instituting a vaccine awareness campaign and also answering any questions. And public health officials really need to go out and calmly discuss the importance of vaccination and how safe IPV is to their patients or to families who are questioning this. And to look back at history and not repeat the same mistakes that we've made previously. Also, just because you don't see polio, doesn't mean it's not here. It is

a silent disease, and we don't want to turn the clocks back to where children can't go out and play in the pool or the lake or the ocean and are stuck at home during the summer with the fear of paralytic poliomyelitis.

Dr. Sarah Hopkins: [34:25] I think I would add to that. One thing that I think is worth considering when we think about AFM versus paralytic Poliomyelitis, we've had since 2014, I think, around 658 cases of AFM, something like that. At the height of the polio outbreaks, paralytic poliomyelitis was happening to tens of thousands of children some years.

Dr. Amy Rosenfeld: [34:59] So the largest outbreak or one of the largest outbreaks that occurred in the United States occurred in 1948 in Kansas City, Missouri and 47,000 children developed forms of paralytic poliomyelitis. And while you can recover, not all of them are able to recover 100% and get movement of the limb back. But there's also a large mental and emotional component of recovery that we didn't track back then. And so, we don't really understand all of that in terms of how the families were affected and how ultimately the child was affected as they moved from childhood to young adult to older adult and now grandparent.

Dr. Sarah Hopkins: [35:57] Yeah, just feels unthinkable now to have 47,000 cases of that kind of presentation in one year. It's amazing.

Dr. Amy Rosenfeld: [36:12] To be honest, when the polio vaccines were discussed about being developed, it was not advocated that there should be a development for a vaccine against poliomyelitis. Many countries were not in favor of this because rotavirus and childhood diarrhea affect millions of children a year. And so, we are very lucky that FDR and Salk and Sabin and all of the pioneers in polio research and the development of the vaccine continued to pursue this and lead us to two effective vaccines. And so now there is no reason for any child or any adult to develop paralytic poliomyelitis.

Dr. GG deFiebre: [37:17] As, I think, Dr. Lockwood talked about earlier, in public health, when things are working and sometimes invisible, we don't see -- when the bad things happen, that's when we see it. So, keeping that in mind of what we don't see, which was the 42,000 cases in a year.

Dr. Amy Rosenfeld: [37:38] This is why I say that in actuality this is the first vaccine any child should get. This is the most important vaccine any child should get because we have conquered this disease and therefore to continue to maintain our ability to conquer this disease, it is imperative that everyone be vaccinated.

Dr. GG deFiebre: [38:08] Any other final thoughts before we end today?

Dr. Katie Lockwood: [38:13] I would just add that with vaccines, having trusted messengers is really important and that's why it's great that you have this podcast to share with your community. But for anyone who's listening who has had a good experience with the IPV vaccine, which should be everyone who's gotten it, talking to your community, especially if you have friends or family members who are hesitant, explaining what you've learned today and your rationale for getting the vaccine and the importance of it, it's really those types of conversations that happen many times outside of the healthcare setting where we aren't that are the most important. And so, if you are in a community with a low vaccination rate, you can be one of those trusted messengers to share how important this vaccine is.

Dr. Sarah Hopkins: [38:58] Absolutely. And I would add that if you're a patient or a family member who is still having doubts, please discuss with your provider. If you're concerned that you're on immunosuppression, call up the person who's prescribing your immunosuppression and have a discussion about this and get your questions answered to move forward and be sure you're protected.

Dr. GG deFiebre: [39:28] Well, thank you all so much for your knowledge, your expertise, and being willing to share this information with our community. We really appreciate it.

Dr. Sarah Hopkins: [39:38] Thank you so much, GG.