

# Polio: Risks for the Posteradication Era

*[Announcer] This program is presented by the Centers for Disease Control and Prevention.*

[Sarah Gregory] Hi everyone, I'm Sarah Gregory, and today I'm talking to Dr. Ananda Bandyopadhyay in Seattle. He is a senior program officer for polio research at the Bill and Melinda Gates Foundation. We'll be discussing his article on the need to prevent risk from poliovirus even after polio is eradicated. Welcome.

[Ananda Bandyopadhyay] Hi. How are you, Sarah?

[Sarah Gregory] Doing well, thank you. Okay so to start off, what is polio and what are the symptoms?

[Ananda Bandyopadhyay] So polio is a disease I love to hate. It's an acute infectious disease caused by a virus, and mostly it is a subclinical infection that we see with polioviruses. So basically, of all the people who are infected with polio, only a small fraction of those infected will show up signs and symptoms of what we call classic paralytic poliomyelitis. And in that small fraction of infected people, it shows up as a disease that causes dramatic onset of paralysis. Typically what we call an asymmetric paralysis, so typically maybe one limb would be affected, and it is sometimes also associated with signs and symptoms of fever, you know, a typical acute febrile illness may be preceding the paralytic onset. But overall, as I said, it's a highly subclinical disease, not everyone who is infected with polio would show up signs and symptoms, but those who do, they would present with paralysis in one part of the body and sometimes more widespread paralysis in multiple parts of the body, as I said acute onset, it's kind of a sudden, a dramatic onset of the illness. And typically, the paralysis with polio is permanent, so there is no cure, really, of the limbs, or the part of the body that is affected with the paralysis. It's typically stays for life, although there could be some improvement with some intervention. And you know, it still remains that prevention is the only way to control polio from spreading and causing paralysis.

[Sarah Gregory] President Franklin Roosevelt had polio, correct? He's a pretty high-profile person.

[Ananda Bandyopadhyay] Yes, so I think the answer would be "probably," because at that time we didn't really have the diagnostic precision like what we have now, in terms of confirming poliovirus infection. And so yes, FDR did have an acute onset paralysis in August of 1921, and the paralysis gradually progressed over the next few weeks. In retrospect, what it seems like, you know, clearly, it was what we call an acute flaccid paralysis, and the paralysis remained, you know, for the rest of his life. It seems like, you know, there could be a few diagnoses that can be made in retrospect from the overall spectrum of his disease, and GB Syndrome is one that also pops up as a possibility. So again, to summarize, probably we'll never know for sure what the causative organism or the pathogenesis was there, but what is really important, Sarah, is his legacy in preventing polio and creating this whole public awareness around the disease. As you know, in January of 1938, he founded the National Foundation for Infantile Paralysis, also

fondly known as the March of Dimes and that innovation revolutionized the whole fight against polio, both from a scientific perspective, you know, this was, you know, one of the platforms that enabled, you know, several scientific research to be continued and supported in vaccine development and eventually became one of them. And, in addition to the scientific innovative development and progress, it also created this whole public awareness and sense of collective ownership in... around fighting a disease, so I think, you know, the legacy part is what really is critically important when we talk about FDR.

[Sarah Gregory] Okay, I'm just gonna—one little point of clarification. You said it was possible that he had GB Syndrome, so for listeners, that's Guillain-Barré, correct?

[Ananda Bandyopadhyay] That is correct.

[Sarah Gregory] Okay. I guess the image of polio is that you get it and you're paralyzed, is that...what you're saying is kind of not actually accurate...but that's why so many people are afraid of it I guess, huh?

[Ananda Bandyopadhyay] Right, so there are a couple of things that we have to understand. One, you know, when we talk about polio, if we're talking about poliomyelitis, the disease, then yes, you know it does affect paralysis, and—and a disease that would, you know, that would be there for life, essentially, but you know the disability would be there for life, typically. When we...when we talk about poliovirus infection, that, as I said, may or may not lead to the disease or paralysis, so you know, roughly, if hundred people are infected with the poliovirus, maybe one out of those hundred infected would develop the classic signs and symptoms of paralysis from polio, the poliomyelitis disease as we call it. The rest would be infected and can still transmit the virus and infect others, but may or may not really show the signs and symptoms of classic polio paralysis. So that's the spectrum of disease and infection, when it comes to polio.

[Sarah Gregory] Okay, your article focuses on the risk of disease after poliovirus is eradicated, but let's sort of...what's the difference between elimination and eradication when we're talking about a disease?

[Ananda Bandyopadhyay] Yeah, that's one of my favorite questions and topics, Sarah. So to put it simply, eradication, you know, typically would need to satisfy a couple of factors, or criteria so to say. So to—again to put it simply, eradication means reduction of disease incidence to zero. This reduction, for our understanding of the science, would have to be permanent, and this reduction, this permanent reduction to zero for disease incidence, will have to be at a global level, it has to hold true when it comes to any and every country in the world. So those three are the primary factors to have a disease, you know, labeled as eradicated. And I'll repeat: it's the permanent reduction of disease incidence to zero at a global level, so all those three basic factors will have to be satisfied, and this is just one meaning of eradication; you could define eradication, or disease eradication, in multiple ways. The basic difference from elimination is probably at the level of geography that we are talking about. So elimination is a term that is used for regional, you know, control of a disease. So if a disease incidence has been brought down to zero in a particular region of the world, then we term it as eliminated from that region. Whenever it becomes true for the entire world, so no country, not even you know, a subnational area, is

reporting any disease of that kind, then it becomes eradicated. So that's kind of the subtle difference between elimination and eradication. To put it simply in polio terms... so for example, the region of Americas has eliminated polio, but of course you know, as a world we haven't eradicated polio. There's only one example of a human disease that has been eradicated and that's smallpox. There's only one other disease that has been eradicated, and that's rinderpest, which is an animal disease. And if you're talking about diseases, those are the two examples that we have successfully eradicated, and out of those two only smallpox is the human disease that was eradicated.

[Sarah Gregory] Okay, could you tell us a little bit about the history of the quest to eradicate polio? It's pretty extensive and dramatic, and why is the diagnosis for polio sometimes missed?

[Ananda Bandyopadhyay] Yeah, great question. So clearly the polio as a disease and, you know, its description we can find in many many literature, you know, going back several hundred years now, we could find, you know, references around, you know, such acute onset paralysis, also reports around epidemics and outbreaks. So it is kind of an ancient disease, so to say. The more concrete reporting of polio and outbreaks of polio probably became apparent around the time of the second. And I think when it comes to a kind of concerted effort to fight the disease as a community, I think the example that stands out is from the time of the inception of the National Foundation for Infantile Paralysis, the March of Dimes that I just mentioned, talking about FDR. So I think that was the time where there was this collective public awareness around the disease and a lot of fundraising activities happened. And that followed the development of the polio vaccines and the licensure of the polio vaccines from mid-1950s when we had the first injectable polio vaccine, which is inactivated polio vaccine, or IPV, developed by Jonah Salk. That came in and then in early 1960s we had the second polio vaccine to be licensed, the oral polio vaccine, or OPV, by Sabin, and then you know, the—you know, it—it remained kind of a fight against the disease with the help of these vaccines at a country level, or sometimes at a regional level, but it (when) it really took a global form was in 1988, when the World Health Assembly passed a resolution to eradicate polio, and that's when the Global Polio Eradication Initiative was formed. And then in parallel and subsequently we saw one country after the other, one region of WHO after the other, becoming polio-free. So the first region that became polio-free was the region of Americas and it was certified as polio-free in 1994, three years after the last child with poliomyelitis was detected. And that saga kind of continued. In fact, the last region to be certified polio-free is the Southeastern region, Southeastern Asian region of WHO, and it was certified polio-free back in 2014. You can see, over several decades, you know, it has been, you know, to start with a country level, maybe a regional level, drive, and then it got transformed into a global push to eradicate. So it has really been a kind of a fascinating quest when it comes to control, elimination, and eradication of polio. Coming to why diagnosis is missed, it again roots back to this issue that you know, it is essentially a subclinical disease, so it's not easy to detect that one case of paralysis out of maybe 99 others who are infected and harboring the virus for the period of infectiousness, so you know we need to have adequate tools in terms of diagnostics to detect poliovirus in those who are infected. We also need to have a program of surveillance in place, so that you know, this detection is done at a population-level, so that whoever is reporting with polio-like illness, which, you know, which includes acute onset of flaccid paralysis, primarily in the younger age groups, surveillance program has the ability to report those cases so that they are investigated and eventually diagnostic methods are applied to confirm or rule out

the existence of poliovirus, you know, from those cases of paralysis. So it is quite a task to continue to maintain that level of sensitive surveillance and then confirm the diagnostic test. The good news is that we have excellent methods of confirming polio. The diagnostic methods that we apply are highly sensitive and specific to detect the existence of poliovirus. It's the question of how the virus presents itself from its transmission pattern, from the fact that it is mostly subclinical, that it becomes a bit difficult to identify areas of virus transmission and eventually confirm cases of poliomyelitis.

[Sarah Gregory] I understand there are three types of wild poliovirus: one has been eradicated, another hasn't been detected since 2012, and the last is currently found only in parts of Afghanistan and Pakistan. So talk to me a little bit about that.

[Ananda Bandyopadhyay] Yeah, Sarah you're absolutely right. So there are indeed three serotypes of the wild poliovirus. It's true—Wild Type II was the first one to be eradicated, out of these three types that we have for wild polioviruses. In fact, it was 1999 that we last saw an indigenous case of Wild Type 2. Essentially, the last naturally-occurring disease with Wild Type II was seen back in 1999, in Aligarh, in a state of—in the state of Uttar Pradesh in India; however, as we report in the article published in EID, there were two cases of Wild Type II detection in the following two to three years, from the period of 2000-2003, there were reports of Wild Type II cases that were possibly linked with a laboratory failure or accident, but it's not confirmed as to how, exactly, that happened. In fact, in 2015, we completed the process of certification of eradication of Wild Type II, so on a lighter note, you know, whenever you are asked how many human diseases we have eradicated, you can mention maybe one-point-three now, now that Wild Type II has been certified eradicated. When it comes to the other two types, again, you are right, Wild Type III has also not been seen for several years now, in fact almost seven years, because we last saw Wild Type III in November of 2012. So that's also possibly gone, but we are keeping a close watch, again, given the subclinical nature, we want to be completely sure that transmission is not happening anywhere, and the good surveillance system of polio gives us confidence around that. The only type that we are now seeing, as we speak, is this Wild Type I of polio. Typically, it's also the type that is known to be most virulent, in other words, it causes more cases compared to the other two types. You know the case to infection ratio, as we call it, for Wild Type I is the highest compared to Wild Types II or III. In other words, the Type II and Type III disease are more subclinical than Type I, it does cause more cases of paralysis, typically, compared to the other two types and this is the wild type that we are still seeing in parts of Afghanistan and Pakistan. Again, you know, it's remarkable that all of the rest of the world, you know, is not reporting any Wild Type I circulation. However, you know, there are still these two countries where we are still seeing active transmission of Wild Type I. That remains a concern.

[Sarah Gregory] Are these wild types, are they the same polio as what we've been vaccinated against? I mean, if I went to Afghanistan, would I be protected?

[Ananda Bandyopadhyay] Yes. The vaccine that we all receive are protective against these types that we're talking about, as long as we have been sufficiently vaccinated or immunized. So, as long as you have completed the recommended doses of the vaccine, then you are expected to be protected against these circulating types of wild virus.

[Sarah Gregory] And you mentioned this earlier—so what is the Global Polio Eradication Initiative? How does it work?

[Ananda Bandyopadhyay] Yeah, so Global Polio Eradication Initiative, or GPEI, is probably the biggest public-private partnership that we have in the world right now. So this was formed back in 1988, as I mentioned, based on a WHA resolution to eradicate polio, and it brought together the global health agencies to enable, you know, the eradication of polio, essentially. So World Health Organization, Rotary International, U.S. CDC, and UNICEF together formed what is called GPEI, and then the Bill and Melinda Gates Foundation joined in this initiative much later, but right now that's what forms GPEI, so you know it's spearheaded by these organizations and it collaborates with national governments, other public and private donors, and constitutes this program, which as I said, is expected to enable eradication of polio, you know, in the near future. So it is—it is a partnership essentially across multiple organizations working very closely with national and regional partners to get to the finish line.

[Sarah Gregory] Are you personally involved in helping to eliminate polio from India? What was your role on the ground?

[Ananda Bandyopadhyay] Yeah, I call myself a foot soldier in the battle to eradicate polio, yes I have been fortunate enough to work in India, to get to elimination of polio. And my shoe leather epidemiology days began essentially right after my medical graduation from Calcutta, which is my hometown in the eastern part of India. That's when I joined the, you know, the National Polio Surveillance Project of WHO. And I worked as a surveillance medical officer in this organization in five states in India when India was intensely endemic, some fifteen years ago. And my role as a surveillance medical officer in WHO was to coordinate large-scale mass vaccination activities and also to monitor disease surveillance initiatives in the remotest corners of the country. So I essentially worked with a team of dedicated and trained professionals who'd—in short, large-scale vaccination activities would happen, and also on the scientific and technical side would support, you know, the detection mechanisms of polio, so the surveillance to search for viruses to ensure adequate reporting is happening whenever a suspected case of polio is being seen, and then streamlining the process of collection of samples from those suspected cases, and confirming in the WHO-recognized labs, the existence or absence of polioviruses from those samples.

[Sarah Gregory] In your opinion, what's been the most challenging part of this effort to eradicate polio?

[Ananda Bandyopadhyay] I think it's reaching every last child in the remotest corners of the world, and doing that consistently over a period of time is what has been most challenging, in my opinion.

[Sarah Gregory] Your study looked at how polio has been accidentally released from labs in real-life experiences from the past eighty years. You were prompted to do this review because of a breach in containment of an inactivated poliovirus, right?

[Ananda Bandyopadhyay] Yes, that's correct. So that breach happened in 2017 in Netherlands, and that was one of the triggers, I would say, to prompt us to do this extensive review.

[Sarah Gregory] How did that happen?

[Ananda Bandyopadhyay] Yes, so as I describe in this report, you know, there was an accidental release from a vaccine manufacturing plant, and essentially from a vaccine production room in Netherlands, and that led to one of the staff who was exposed to be infected with the wild virus strain, and apparently the person tested positive for several weeks for virus post this exposure, and then, you know, what it really means is that once you're detecting virus in an individual, you know, essentially through the testing of the stool samples, among other samples from the individual, it means the community around that individual is also potentially at risk of being infected or, you know, diseased, essentially, depending on the vaccination status of the community. So it is a matter of major public health importance to detect such an incident in a timely manner and then monitor, you know, the shedding from such individuals so that the community risk is minimized. And also this is linked, as I said, with the background vaccination status in the place where it is happening. So, overall, this was a quite an important public health event and we wanted—based on this, we looked back on other incidents of such laboratory, you know, accidents or leaks that might have happened. So we went back and essentially looked into nearly past eight decades of such incidence and we summarized our findings.

[Sarah Gregory] Back to your study, what did you find? Were there any patterns?

[Ananda Bandyopadhyay] Yeah, so we did this study as a collaborative effort, first of all. So, I joined forces with my colleagues at World Health Organization and also other colleagues within the foundation's polio team to complete this review. We found around twenty-nine references in the scientific literature, in this period of roughly about eight decades or so, where the rare documented release of poliovirus in different—from different settings of laboratory to vaccine production units and so forth. And what we zoomed into was this period of 1933 to 2017, so quite a long period, as you can imagine. In terms of patterns, you know, there was at least one distinct pattern that we could observe, which is related to, you know, whether or not this is happening in the pre-vaccine era, more precisely in the pre-GPEI era, or not. But typically, what we found was that incidents that happened in the pre-vaccine or pre-GPEI era were primarily related to the research facilities, and we have to take into consideration here that surveillance for polioviruses and diagnostic capabilities to detect polioviruses were not as optimum as they are right now. So there is that surveillance artifact in this assessment. But typically, the impact of release, in terms of paralytic disease or virus transmission, would be significantly more in the pre-vaccine era. When it comes to reports in the post-vaccine era, or as I said, more focused around the post-GPEI era, which is roughly about three decades or so, the pattern typically is of an accidental release primarily from the vaccine manufacturing facilities or laboratories handling polioviruses. And the impact, typically, in terms of the number of cases of paralysis, is much much less than what we would see in the pre-vaccine era. And of course the community, you know, in a way, is way more well-vaccinated against polio now than what it used to be in those decades of 1930s, 40s, and so forth. And to add to that, our surveillance capabilities are also way more enhanced now than what it was back then. So, not only we have surveillance for acute flaccid paralysis, or AFP surveillance as we call it, we also now have environmental surveillance

as an option of polio surveillance. And essentially it's becoming more and more important. So all those factors come in when we try to assess both the public health impact and also the way we monitor such accidental releases. That was quite striking, you know, the difference between the pre-vaccine, and in a way, the pre-program era, to the post GPEI-era of the past three decades or so when it comes to how many cases you see post such accidental releases, and also how you detect and monitor over a period of time post the incident has occurred.

[Sarah Gregory] Were there any incidents that particularly fascinated you in this history?

[Ananda Bandyopadhyay] I think there were many incidents that were quite intriguing, starting off from the first one in 1933 to the last one, you know, that we documented in 2017. Probably more because it's so close to our current activities of eradication and also happening in an era when this particular country, Netherlands, you know, has been polio-free for several years and the region is also polio-free. So a release that happens in a setting like this, when you're already in a post-elimination setting in the country or in the region, the implications are quite fascinating. And also how you actively monitor the risk to the community is also the other part that intrigued me. I think the third factor in here is, you know, we are dealing, in this case, with Wild Polio Type II, which, as I said, is something that has been certified eradicated. So, you know, the implications of that is also quite fascinating. So I think, overall, the last incident would probably stand out as the most fascinating one to me, although there were several, as I said, which were quite interesting.

[Sarah Gregory] Today, what can we learn from these past incidents? What are the most important steps that need to be taken post-eradication to prevent additional releases?

[Ananda Bandyopadhyay] I think that's a very important issue for discussion. I would categorize the things that we could learn into three broad areas, really. I think the first step is to ensure there is a uniform and global awareness around the importance of implementing the Global Action Plan 3, as we call it, or GAP 3 guidelines, to ensure that we minimize the facility-associated risks of re-introduction of polioviruses. So containment measures need to be there is extremely important. And as I said, certain awareness has to be at a global level and, you know, at a uniform pattern. The next issue, I would say, is to ensure that there is a method in place regarding potential infectious materials for polioviruses in all facilities that probably store human stool specimens or respiratory samples, or even environmental sewage, for that matter. Because as I said, all could potentially harbor polioviruses. In listing such facilities and materials within such facilities and tracking them and taking necessary actions, if needed, is an important step. The third one, which I think is kind of an overarching one and still very important, is the approach to optimize the measures of containment so that we still can encourage critical vaccine research and development activities to move forward. Just as an example, we are developing with partners, you know, new oral polio vaccine which is supposed to be more stable. We are also partnering with several research organizations and agencies to develop antiviral drugs against polio. These are all keeping in mind, you know, to minimize the risk of post-eradication era and in order to ensure timely development of these vaccines, we need to, as I said, optimize the measures of containment and how we ensure that at one hand, adequate containment measures are in place to minimize any chance of reintroduction of polioviruses. On the other hand, we optimize such measures on a case-by-case basis so that the development and research

activities can go on so that, in the long run, we have potentially safer alternatives to maintain polio eradication for long term. So I think, to me, those three are the key takeaways or lessons learned when we look back in some of these incidents.

[Sarah Gregory] Would it be possible that polio might make a resurgence?

[Ananda Bandyopadhyay] Well, as I said to start with, polio is a highly contagious disease. And any infectious disease is a plane ride away, as long as it is there somewhere. What is critically important is to maintain immunity in the population, which comes through vaccination. So as long as we maintain adequate vaccination and keep the population immunized, then the chance of a resurgence are extremely less. But yes, it is a possibility, particularly if vaccination rates fall, you know a poliovirus reintroduction can lead to transmission very easily.

[Sarah Gregory] After polio is eradicated, you're saying people should still need to be vaccinated against it, but be not vaccinated against smallpox?

[Ananda Bandyopadhyay] Correct, so it all depends on the time window that we're talking about. So post-eradication could be immediate short-term post-eradication and recently SAGE has recommended the period to be roughly ten years. So that would be probably the time period when people would still need to be vaccinated. Whether or not it needs to be continued for longer, I think that remains to be discussed and evaluated as we get closer to the eradication timeframe. But, overall, the principle would be that beyond a specified timeframe, we will probably not need to be vaccinated forever. I think that's probably what we are looking at. So again, to summarize, immediate post-eradication or post-certification period, the vaccination activities will have to continue, it might be ten years, might be more for certain countries or regions where there are sources of polioviruses within facilities. But beyond that, it's possible that we'll stop vaccination and will maintain a world free of polioviruses.

[Sarah Gregory] Okay. And what do you personally feel is the number one or number two things people can do to protect themselves from diseases. All diseases, not just polio.

[Ananda Bandyopadhyay] I think number one, two, and three are all vaccination, if you ask me. I think that is the core of us staying protected against the threat of such infectious diseases. It is the most powerful tool that we have, most cost-effective tool that we have for disease prevention. And I think I would keep it, you know, at vaccination, period. So vaccinate and keep the population immunized—that is the central thing that we all could do to protect ourselves against such diseases.

[Sarah Gregory] Do you think that we can actually eradicate polio within our lifetimes?

[Ananda Bandyopadhyay] Oh absolutely. We can, we should, and we have to. You know, we can because we have the tools, there is proof of concept, more than 99 percent of the world is free of live polioviruses, as we've discussed. There's only the two countries that we mentioned which actively are reporting wild polioviruses as we speak, but the rest of the world is free. You know, and thanks to the vaccination activities, thanks to the eradication program to make that happen, so absolutely we can. We should because it's the only way to wipe the virus out forever, and



prevent any child from getting paralysis ever again. And I say we have to because we are very very very close to the finish line, and the success here would really set the platform for other diseases to be potentially eradicated or eliminated. There are challenges, and there are significant challenges in the places where wild poliovirus is still there. But they can be overcome, as we have demonstrated in other areas of the world. So we can really do this as a global community and get rid of the disease once and for all.

[Sarah Gregory] What first inspired you to join this effort to eradicate polio?

[Ananda Bandyopadhyay] Thanks for asking this, Sarah. I think it was the power of vaccines and vaccination that were instrumental in kind of inspiring me to join this effort. I think the science behind how a vaccine works inspired me as a medical student. And then the art and act of vaccination, you know, the art and act of saving lives, I think that fascinated me as a young field epidemiologist working in India. I was also deeply deeply inspired by the courage and the spirit of countless vaccinators who'd walk barefoot for miles in very difficult conditions, be it flood, be it other natural disasters, or just difficult geographies. And they would go house to house to immunize each and every children in their designated areas. I somehow felt I was closer to the ground reality of the nation, you know, with such kind of work, and also of its people than I was ever before, you know, growing up in a city like Calcutta. So, overall, the program has reached the unreached; it is quite remarkable. And I think that resonates with public health officials like me.

[Sarah Gregory] Okay, and finally tell us about your job at the Gates Foundation.

[Ananda Bandyopadhyay] I'm a senior program officer in the polio team. I focus on polio research, so I partner with several within the foundation, several experts within the foundation, and also outside the foundation I team up with our core partners at GPEI, or externally, partners at universities, and other research collaborators, to drive the research and development work for polio eradication forward. So I focus on several vaccine studies to look into the existing vaccines and try to come up with ideas and ways to improve the immunogenicity of the existing vaccines, depending on when we use it and how we use it. A focus of our research is also around affordability and accessibility of the existing vaccines, so how we can deliver the existing vaccines to the underserved populations is a core area of the research, as well. We also focus on developing new vaccines, so even though we have two vaccines in place, whether or not in this peri-eradication era, or the post-eradication era, you know, there would be new improved vaccines that could help us maintain the eradication of all types of polioviruses, is again a core research area. And we also focus on other research initiatives, like and around surveillance enhancement and so forth, and so all of this, there are major partners of research, as I said, within the polio team and outside who I work with. Essentially it's a team effort of the foundation, partnering with others to help make progress on the eradication front.

[Sarah Gregory] Thank you so much for taking this time to talk with me today.

[Ananda Bandyopadhyay] Thank you, Sarah, it's been a pleasure.

[Sarah Gregory] And thanks for joining me out there. You can read the July 2019 article, “Facility-Associated Release of Polioviruses into Communities—Risks for the Posteradication Era” online at [cdc.gov/eid](https://www.cdc.gov/eid).

I’m Sarah Gregory for *Emerging Infectious Diseases*.

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