

Vaccines Are Bringing Back a Nearly Eradicated Deadly Virus

BY Xiaoxu Sean Lin and Health 1+1 (Epoch Times)

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Many people thought that the poliovirus was extinct across the majority of the world, as the World Health Organization (WHO) has declared many continents polio-free. So, this may come as a surprise, but in fact, polio cases have been on the rise globally since 2016, and this resurgent outbreak is related to the use of vaccines.

On July 21, 2022, the first polio case in almost one decade was reported by the New York State Department of Health. And this case was also related to a vaccine-derived poliovirus strain. Poliovirus is non-enveloped. It is an enterovirus composed of a single stranded RNA and a protein shell.

Roughly 3 in 4 people infected with polio are asymptomatic. Even if there are symptoms, they usually resemble those of a flu. Yet in 1 percent of all polio cases, polio causes flaccid paralysis or disability, and it even can lead to death. This is then called paralytic poliomyelitis.

After contracting spinal paralytic poliomyelitis, 25 percent to 40 percent of patients will develop varying degrees of sequelae up to 15 to 40 years later, which are also known as “post-polio syndrome.”

This may be because when some patients are young, their immune system is quite strong and able to inhibit the replication of the poliovirus. As they get older, their immunity tends to decline, and the virus within their body may return to wreak havoc. If the virus affects the neurons or muscles, then it may, in severe cases, lead to temporary or even permanent paralysis or disability, as well as reducing the respiratory muscle function and even causing breathing to stop, which then leads to death.

Why Is Polio Reemerging After Being ‘Eradicated’?

In the 1950s, polio became a global concern. In 1955, the inactivated polio vaccines (IVP) were developed; and in 1962, the oral poliovirus vaccines (OPV) were invented.

In 1988, the WHO, United Nations International Children’s Emergency Fund (UNICEF), and Rotary Foundation launched the “Global Polio Eradication Initiative (GPEI),” with the Bill and Melinda Gates Foundation as the major funding institute. Primarily through global distribution of polio vaccines (especially in developing countries) in conjunction with education and prevention campaigns, GPEI hoped to eradicate polio completely. The WHO has since granted certificates to many countries and regions to prove that they have eradicated polio.

The United States eradicated polio in 1979, and the Americas were the first region in the world to become certified polio-free in 1994. Afterwards, the Western Pacific Region, Europe, Southeast Asia, and Africa were certified polio-free in 2000, 2002, 2014, and 2020, respectively.

Mainstream media and public health agencies worldwide have unanimously and loudly praised the GEPI and give all the credit of polio eradication to the vaccines and GEPI. However,

realistically speaking, the circulation of poliovirus in the world also has its own patterns, with peaks and declines with or without people's intervention. As a matter of fact, global polio cases entered a sharp decline phase from the late 1950s before the inactivated polio vaccine was widely distributed and before the oral polio vaccine was even invented. When GEPI started in 1988, there were only several tens of thousands of polio cases globally. Indeed, the extent to which polio vaccines actually worked to control polio outbreaks on a large scale has not been tested in practice.

Furthermore, the WHO's "polio-free certification" only targets the wildtype strains of the poliovirus. In 2016, the number of polio cases, which dropped to its lowest in decades, saw a sudden increase. And this time, the poliovirus strains that caused the outbreak were related to the vaccines.

Oral Polio Vaccines Can Cause Poliovirus Transmission

Since the oral poliovirus vaccines (OPV) were produced with attenuated poliovirus strains, the viruses were not dead in the vaccine. They were just attenuated to lose neurovirulence and had reduced transmissibility. However, when the OPV were promoted in many developing countries, the less virulent strains could replicate silently for a long time in people who take the OPV. In rare occasions, the attenuated poliovirus could revert and replicate efficiently again, or even become virulent again, especially among people who have weak immune systems.

This is because the OPV uses a traditional virology technology to reduce the virulence and productivity of the virus instead of killing it. When the "weakened" viruses from the OPVs enter human intestines, it is possible for some to mutate and regain their neurovirulence. These types of viruses are called vaccine-derived polioviruses, or VDPVs.

These vaccine-derived viruses are transmissible among humans. And they can cause the patients to develop symptoms such as paralysis and disability. This condition is called vaccine-associated paralytic poliomyelitis (VAPP). The VAPP risk of a newborn is 4.7 cases per million.

According to data from Our World in Data, nearly 80 percent of 1-year-old infants around the world have received the polio vaccines since 1990. The most used vaccines were still the OPVs at the time. This means that if 100 million children were born, and 80 million received the OPVs, then there could be 376 VAPP cases.

Vaccine-derived Polioviruses Started to Spread After 2016

There are 3 types of polioviruses, including types 1, 2, and 3. The original version of OPVs included all three types; and all three serotypes of attenuated strains can generate revertant VDPVs respectively. However, the revertant VDPVs-2 (type 2) strains were more dominant and have been the main circulating VDPV strains (cVDPV-2).

After this issue was discovered in 2016, the WHO made a decision to stop the production of the OPVs with all three types. Instead, the newer version of OPV for wide distribution included only serotypes 1 and 3. And OPV-2, a newer version of OPV with only type 2, was also produced separately to be used in poliovirus type 2 endemic areas.

However, this “switch” from trivalent to bivalent OPV vaccines resulted in unexpected problems again. After using the OPV with types 1 and 3 (bivalent OPV vaccine), the outbreak of cVDPV-2-related polio cases increased significantly from 2016. This appears to suggest that the cVDPV-2 has been circulating at low levels before the switch was made in 2016. So, the switch actually took away the pressure against cVDPV-2 and gave it more chances to cause small scale outbreaks in many regions of the world. And now, the overall polio virus cases worldwide are back to the level of 20 years ago, even though more continents and countries are declared “Polio-free” ironically.

The main reason that the OPV was still being used widely is that OPV can be produced and offered at a low cost, which would benefit the distribution to the developing world. In addition, OPV can stimulate mucosal immunity in the intestines better than the inactivated vaccine. Therefore, it has always been assumed that OPV can reduce the poliovirus transmission more effectively than inactivated vaccines, although no related tests have been done for any of the newer versions of the OPV.

In fact, if the inactivated polio vaccines (IPVs) were used instead of the OPVs, then there wouldn't be this problem of generating circulating VDPVs. Developed countries, including the United States, have all stopped using the OPVs since 2000, and they all use the IPVs.

This creates a dilemma: on the one hand, developing countries can only use OPVs to prevent and control outbreaks; but on the other hand, OPVs can cause further spread of the viruses.

Can the New Oral Poliovirus Vaccine Also Mutate?

It is well established that the wild type poliovirus has high mutation errors during its replication cycle, however, it is not known clearly whether the attenuated virus strains in the original OPV had a mutation rate as high as the wild type virus.

The frequent appearance of VDPVs suggested that the mutation rate was still relatively high in those attenuated strains. Therefore, the scientific community set out in 2010 to work on a new version of OPVs, which are not prone to mutation. They made many modifications to the type 2 poliovirus genome, including mutations within the 5'-untranslated region (UTR), the RNA-dependent RNA polymerases, and other important regions. These mutations were confirmed in in vitro experiments to reduce the error rate of the virus replication process and make the virus less prone to mutation. Later, this novel OPV (nOPV-2) was demonstrated to be well-tolerated, have noninferior immunogenicity, and better genetic stability compared with original monovalent type 2 OPV. Studies on transgenic mice showed significantly lower neurovirulence of fecally shed vaccine virus.

So, nOPV-2 was quickly commercially produced in hopes of reducing the risk for generating VDPVs and the risk for vaccine-associated paralytic poliomyelitis cases.

Based on the public health emergency of international concern generated by ongoing endemic wild poliovirus transmission and cVDPV type 2 outbreaks, the WHO authorized nOPV2 for use under the Emergency Use Listing (EUL) pathway in November 2020, allowing for its first use for outbreak response in March 2021.

However, based on a surveillance report on 2021 during the initial phase usage of nOPV-2 from March to October 2021, the genetic characterization of the vaccine-related poliovirus strains showed that across 251 VDPV isolates analyzed in this study, mutations altering RNA secondary structures, as well as capsid mutations affecting antigenicity and attenuation were all observed. And mutation combinations (including the A481G reversion) identified in nOPV2 isolates would cause the nOPV2 strain to approach the neurovirulence of wild type poliovirus-2. Therefore, the nOPV-2 still expressed safety concerns even though it is widely used in some African countries now.

With all these challenges and unexpected disasters of circulating virus revertants, we need to ask seriously: Is eradicating poliovirus a realistic objective? As a matter of fact, GEPI primarily relied on vaccine campaigns. However, vaccines are not medications, and they don't function to "kill" a virus. It only helps to stop transmission of the virus in ideal situations. We don't know of any other natural animal reservoirs for the poliovirus to hide, outside human hosts. How could we "eradicate" a certain virus with vaccines when we don't know where the virus comes from?

Are we creating more problems with a wrong objective coupled with a wrong approach?

On the one hand, people want to wipe polio out from the face of the earth, yet on the other hand, the vaccines are "spreading" the viruses all over the world. The VDPVs are still polio viruses, even though they are not wild type polioviruses. Delta or Omicron variants are still SARS-CoV-2 viruses, even though they are not the wild type Wuhan strain. Are we fooling ourselves by declaring some regions or countries as polio-free, simply based on not detecting wild type poliovirus, while we clearly know that VDPVs are still circulating, and even spreading faster due to the large OPV campaigns in many developing countries?

With billions of dollars spent on GEPI globally, with many intensive campaigns to inoculate people, especially children, with OPVs (regardless old or novel versions), we are inoculating the world with more VDPVs in nature as we have no way to contain its existence and spread. Is eradicating polio becoming a delusion that the world just cannot wake up from, as we have invested so much of money, emotion, effort, and dedication to it, even though we know that the train is on the wrong track?

In fact, epidemics have their own patterns. As mentioned earlier, the global polio epidemic was already on the decline before the vaccines were rolled out. During the COVID-19 pandemic, as dose after dose of the vaccines were administered, the pandemic continued to rise and fall, and the SARS-CoV-2 virus also kept mutating. The vaccines didn't seem to be able to reverse the trend of the pandemic or stop the virus from mutating. If we can calm down and not just blindly treat vaccines as the only solution, we might be able to find a better way to prevent future pandemics. We did not learn the lessons from the polio and the GEPI, so we are repeating the efforts and the mistakes on campaigns against COVID-19, and we probably will repeat it on another future outbreak, again and sadly.

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