nature

Why is vaccine-derived polio so hard to stamp out?

Research published this week adds to the toolkit against vaccine-derived poliovirus. But novel vaccines will not work if they remain in their vials.

When smallpox was declared eradicated in 1980, there were hopes that poliovirus might soon be next. As a result of an eradication campaign that began in 1988, two of the virus's three subtypes have since been eradicated and the third has been cornered. In the past 12 months, just 21 cases of wild polio were reported in children across Afghanistan, Pakistan and Mozambique.

But cases of another type of polio are worryingly high. Over the past year, there have been 665 cases of vaccine-derived polio across 23 countries. Vaccine-derived polio occurs when the attenuated poliovirus used to make oral vaccines regains its virulence.

In *Nature* this week, Andrew Macadam at the National Institute for Biological Standards and Control in South Mimms, UK, and his colleagues report the development of novel oral polio vaccines that reduce the likelihood of vaccine-derived outbreaks occurring for poliovirus types 1 and 3 (ref. 1). These vaccines were created using an approach previously used to make a new type 2 polio vaccine known as nOPV2 (ref. 2). The scientists used genetic engineering to slash the likelihood that the attenuated virus will revert to virulence. The two latest vaccines were tested in mice and found to be effective, safe and stable. They are now being tested in human trials. If their safety and efficacy are as good as that of the nOPV2 vaccine, all three poliovirus subtypes will be covered.

Since March 2021, the nOPV2 vaccine has been administered to more than 650 million children across 30 countries. But although nOPV2 is much more stable genetically than its predecessor, it can regain virulence, too. So far, it has done so on four separate occasions, in Nigeria and the Democratic Republic of the Congo. This is probably because eradication campaigns are not reaching enough children, and it reinforces what researchers and public-health officials already know: for polio to be eradicated, advances in science need to go hand-in-hand with comprehensive public-health initiatives.

The rise in the number of outbreaks of vaccine-derived polio has various causes. The COVID-19 pandemic hindered vaccination campaigns and surveillance. Disasters and conflicts, which often occur in countries vulnerable to polio, have done the same. Moreover, some countries decided to delay their outbreak responses and wait for supplies of the nOPV2 vaccine, rather than use the older type 2 vaccine. A modelling study, originally published in 2021, suggested that this delay would increase the risk of outbreaks occurring[3].

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High-level changes to the way in which polio campaigns are run is another factor underlying the deterioration of some campaigns, according to several researchers that *Nature* spoke to for this editorial.

Around the world, polio eradication has long been handled by the Global Polio Eradication Initiative (GPEI), a partnership based in Geneva, Switzerland, that includes national governments, philanthropic funders and the World Health Organization. However, the WHO is now overseeing a plan to transfer some of the GPEI's activities to national immunization and disease-surveillance programmes. This has involved the GPEI handing over some responsibility to the WHO, and the WHO then helping national programmes to manage independently.

The transition has not been easy. There have been funding gaps, expert staff have been lost, governance has faltered in some countries and morale has dropped in others. A report published in April 2022 by the Independent Monitoring Board (IMB), a group of global-health experts that the GPEI commissions to produce periodic assessments of progress, has been critical of the transition process in some countries (see go.nature.com/3qhjk6a). A WHO spokesperson told *Nature* that the transition programme accepts that it "pulled the plug too early in some of these countries", and said that it is drawing up a country-by-country approach.

The publication of a new independent report later this month will reveal more about how the transition is going. In the long term, it makes sense to integrate the GPEI's formidable polio resources into national immunization programmes. But it is crucial that this be done in a way that does not undermine the progress already made. The GPEI needs to remain in the picture.

Meanwhile, scientists have other tools in the pipeline to further the polio-eradication campaign. At present, it can take many weeks to confirm that a wastewater sample contains poliovirus. Several research groups are working on technologies to reduce this time lag. Separately, Macadam and his colleagues are developing a form of the virus that is inactive *in vivo*. They hope this could one day replace the infectious virus that is currently used to make vaccines.

It's essential that researchers continue to advance vaccine research and technology to combat the rise of vaccine-derived polio. But new vaccines will not work if they remain in their vials. If the world is to see the back of vaccine-derived polio, the fruits of vaccine research and development need to be put into the hands of highly motivated, well-funded staff operating in programmes attuned to the local landscape, and the transition of polio management from the GPEI to national control must not undermine eradication. Only then might we be able to send polio the same way as smallpox.

1. Yeh, M. T. *et al. Nature* https://doi.org/10.1038/s41586-023-06212-3 (2023).
2. Yeh, M. T. *et al. Cell Host Microbe* **27**, 736–751 (2020).
3. Kalkowska, D. A., Pallansch, M. A., Wassilak, S. G. F., Cochi, S. L. & Thompson, K. M. *Vaccine* **41 (Suppl. 1)**, A136–A141 (2023).