Polio eradication at the crossroads

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The Global Polio Eradication Initiative, launched in 1988 with anticipated completion by 2000, has yet to reach its ultimate goal. The recent surge of polio cases urgently calls for a reassessment of the programme’s current strategy and a new design for the way forward. We propose that the sustainable protection of the world population against paralytic polio cannot be achieved simply by stopping the circulation of poliovirus but must also include maintaining high rates of population immunity indefinitely, which can be created and maintained by implementing global immunisation programmes with improved poliovirus vaccines that create comprehensive immunity without spawning new virulent viruses. The proposed new strategic goal of eradicating the disease rather than the virus would lead to a sustainable eradication of poliomyelitis while simultaneously promoting immunisation against other vaccine-preventable diseases.

Introduction

Inspired by the previous success of smallpox eradication, the Global Polio Eradication Initiative (GPEI), launched in 1988, was aimed for completion by 2000. The initial strategy was based on stopping transmission of wild polioviruses by global coordinated use of the trivalent oral poliovirus vaccine (OPV), which was to be followed by the destruction or containment of all stocks of poliovirus and the stopping of immunisation. This step was expected to prevent rare (one in a million) cases of vaccine-associated paralytic poliomyelitis (VAPP) and to allow the redirection of public health resources to other priorities. Early progress was tempered by the observation that the attenuated virus can revert to variants leading to the emergence of circulating vaccine-derived polioviruses (cVDPVs) with pathogenicity and transmissibility indistinguishable from those of wild polioviruses. Most cVDPV strains are of serotype 2, and most are recombinants between different serotypes of attenuated polioviruses or with other non-polio human enteroviruses. As the circulation of wild polioviruses dwindled, the importance of cVDPVs increased, and they now cause the majority of paralytic polio cases in the world. The distinction between cVDPVs and wild polioviruses is purely academic because they both transmit readily in poorly immunised communities, cause outbreaks of paralytic disease, and their presence requires the same programmatic response. The inevitable emergence of cVDPVs means that polio eradication must also include elimination of OPV itself, at least in its present form, which substantially complicates the original task.

Another obstacle to eradication was the extraordinary persistence of wild poliovirus circulation in some geographical regions. Military and political conflicts in some parts of the world limited access to children by vaccination teams. In other regions, unfounded prejudices regarding vaccine safety caused refusals of immunisation. Observations in India at the turn of the century showed that in some regions immunogenicity of trivalent OPV was very low, which was caused by a high prevalence of other enteric infections, and interference between serotypes of vaccine virus in trivalent OPV: the OPV type 2 (OPV2) component of trivalent OPV reduced immunogenicity of the other two vaccine strains; therefore, each child had to be vaccinated up to 50 times to reach the population immunity threshold required to stop virus circulation. To increase the immunogenicity of the vaccine, monovalent OPV type 1 (OPV1) and OPV type 3 (OPV3), and a bivalent OPV containing only serotypes 1 and 3 were introduced for supplemental immunisation campaigns. The introduction of these new vaccine formulations finally led to the cessation of transmission of wild type 1 poliovirus in India, but the downside was a reduced immunity against serotype 2, which promoted the emergence of type 2 cVDPV (cVDPV2).

The global resurgence of cVDPV2 that started in 2016 was associated with the switch from the use of trivalent OPV to bivalent OPV not only for supplemental immunisation but also for routine immunisation implemented after the declaration of global eradication of wild type 2 poliovirus. It created substantial gaps in population immunity to type 2 poliovirus, providing fertile grounds for cVDPV emergence. As a result, the number of paralytic cases caused by cVDPV2 has been steadily increasing in many countries in Africa and Asia. In this Viewpoint, we attempt to make some recommendations that might help to put the eradication programme back on track for sustainable success. Over its history, the GPEI continuously made policy adjustments, and elements of our proposal have been previously discussed, and some are being implemented. Nevertheless, there is an urgent need to integrate all new ideas into a comprehensive and sustainable general strategy, which is the main objective of this Viewpoint.

Refocus eradication campaign priorities

Since its outset, the GPEI strategy focused primarily on stopping virus transmission to prevent paralytic poliomyelitis; the measure of its success was on the basis of the absence of paralytic disease and asymptomatic circulation of live poliovirus. A crucially important aspect of this approach is the destruction or secure containment of all poliovirus stocks. However, we posit that this strategy is unrealistic and undesirable, and should be replaced with emphasis on protecting the global
population by continued immunisation with safe and effective vaccines. The rationale is two-fold. First, proving the absence of poliovirus circulation is a daunting task that cannot be verified reliably because of the limitations of existing surveillance tools, which include acute flaccid paralysis surveillance supplemented by environmental surveillance. Surveillance of acute flaccid paralysis is based on clinical manifestations of poliovirus infection, which worked well in the initial phases of polio eradication. In a fully susceptible population, acute flaccid paralysis surveillance can detect one in 100 to 1000 infections. However, with increasing population immunity, surveillance for clinical signs of poliovirus infection becomes much less sensitive, allowing poliovirus to circulate undetected for many years. Combined with the poor implementation of acute flaccid paralysis surveillance in some regions, this occult circulation was the reason for the emergence of the so-called orphan poliovirus lineages that resurfaced after many years of circulating undetected. Although environmental surveillance is believed to be more sensitive than acute flaccid paralysis surveillance, its global implementation is unrealistic because of the enormous cost and the absence of sewage systems in substantial parts of the world where environmental surveillance is needed most. For the current eradication strategy to work, effective surveillance must be done not only as part of a one-time certification process but must be continued into the future. Therefore, ensuring that there is no silent poliovirus circulation is next to impossible. Second, a fully secure containment of poliovirus is unrealistic because it can be easily recreated in a test tube and will remain a threat to humankind, similar to other human pathogens that can be synthesised. A drastic resurgence of the disease could occur in a fully susceptible population if a single infectious virus enters circulation. Therefore, failure to maintain high immunity to poliovirus would create unacceptable vulnerability, potentially leading to a global catastrophe.

At the core of our recommendation is the replacement of the goal to globally eradicate poliovirus with an emphasis on protecting populations from paralytic disease caused by poliovirus. The only sustainable solution to eliminating paralytic poliomyelitis is to indefinitely maintain the highest possible rates of population immunity through quality immunisation programmes. If and when new vaccines inducing comprehensive immunity without causing VAPP and cVDVPVs become available, conventional OPV must be phased out. However, until the new vaccines are available, conventional OPV must continue to be used. The objective of our efforts should be to eliminate the disease, not the virus. A limited transmission of poliovirus might still occur and should not be considered a failure of the campaign. Importantly, the proposed strategy does not abandon the goal of eradication because after sustainable vaccination programmes are in place worldwide, strong population immunity will ensure that the virus will no longer be able to transmit and will gradually disappear.

The emphasis on universal vaccination rather than on hunting down each chain of transmission will provide substantial relief and benefits to the programme by making some current activities unnecessary or less crucial. The Global Action Plan that codified very strict containment measures was developed and implemented on the premise that immunisation would stop after eradication is declared and polio immunity will decline. A new emphasis on vaccination programmes, as opposed to virus circulation, and the return of trivalent OPV in combination with inactivated poliovirus vaccine (IPV) or a new genetically stable version of the vaccine that is crucial to stopping the current surge of cVDVPV2 will make draconian containment measures unnecessary, thus eliminating an undue burden on the pharmaceutical industry and enabling badly needed research and development to expand the availability of critically needed polio vaccines and antivirals.

Do not stop immunisation, improve its quality

The arguments made so far make it clear that immunisation against polio must be continued indefinitely. This proposition is widely accepted by high-income countries that have no intention to stop vaccination against polio. However, resource-limited countries rely on international aid to sustain vaccination efforts. Although the original scenario of abandoning all polio immunisations was gradually replaced with a plan to switch from OPV to IPV after detectable circulation of poliovirus is stopped, the 2019 WHO recommendation specifies that this switch is only an interim policy and that, at some point, IPV might become unnecessary. Besides putting at risk people in low-income countries who constitute the majority of the world’s population, this position has other important flaws, both practical and ethical. Limiting the horizon of polio vaccine use to only a few years discourages investment in the development of new effective vaccines. The proposition also contains an unacceptable double standard for the protection of populations in high-income and low-income countries. Therefore, the prudent, sustainable, and equitable solution would be to continue polio vaccinations indefinitely.

A preview of what would happen if polio immunisations were stopped was provided by the switch from trivalent OPV to bivalent OPV use. This switch was supposed to be accompanied by the global introduction of IPV to maintain immunity against type 2 poliovirus. Aside from the fact that IPV cannot stop the spread of poliovirus because of its inability to generate adequate mucosal immunity, at the time of the switch, there was a severe shortage of IPV so that large cohorts of newborn babies were left unprotected. The switch was hastily implemented despite the continuation of cVDVPV2 outbreaks and was based on modelling, which...
At present, several approaches could be a better solution than the introduction of a new vaccine. Withdrawing protection against disease when effective vaccines are available demands considering all possible intended and unintended consequences. A growing body of evidence suggests that besides protecting against their target pathogens, many live vaccines also exert non-specific effects on the basis of stimulation of innate immunity that prevents other infections. OPV has been shown to decrease the incidence of seasonal influenza, bacterial diarrhoea, and otitis media, and was found to reduce all-cause childhood mortality by as much as 30%, even in the absence of poliovirus circulation. By some estimates, increased mortality after the withdrawal of OPV and its replacement with IPV could be higher than the number of VAPP and cVDPV cases that the measure would prevent. Despite these multiple observational studies, the off-target protective effect of OPV remains a controversial subject that demands active research, including mechanistic and prospective clinical studies with new genetically stable OPV. But withdrawing OPV without getting a clear answer based on solid science would be irresponsible.

**urgent action needed**

In this Viewpoint, we propose a long-term strategy to achieve sustainable eradication of poliomyelitis. In the meantime, there is a crucial need to close the gaps in population immunity and prevent explosive multiplication of cases such as those induced by cVDPV2. To do this, the programme should withdraw the use of bivalent OPV globally and abandon any plans to use monovalent OPV1 or monovalent OPV3 for routine immunisation, because this strategy can be predicted to result in the proliferation of type 1 and type 3 cVDPVs, as was already shown for cVDPV2. To increase population immunity and stop the spread of cVDPV2, sequential immunisations with IPV and trivalent OPV, a strategy already used very successfully in many countries, should be introduced in countries that currently use bivalent OPV. This regimen has been proven to induce a durable and comprehensive immune response while minimising the chances of paralytic poliomyelitis. Although sequential immunisation might have operational challenges in some parts of the world, it could be used as an important stopgap measure to prevent the spread of cVDPVs until a permanent solution, such as a genetically stable novel OPV, is available for implementation.
Conclusion

Permanent elimination of the threat of paralytic poliomyelitis caused by poliovirus cannot be guaranteed by hunting down the virus, and can only be achieved by maintaining a high rate of population immunity. The approach proposed here focuses on preventing disease rather than getting rid of the virus. This approach will help move the programme forward, guided by new benchmarks of success focusing on disease.

The modified strategy should be a part of the next phase of the polio eradication campaign that should better synergise and be merged with other global immunisation programmes. Although the history of the campaign clearly shows that success cannot be guaranteed regardless of how close it appears to be, we believe that this new strategy will lead to a sustained elimination of paralytic poliomyelitis caused by poliovirus.

Contributors

All authors contributed equally to the conceptual development of the proposal and writing the manuscript.

Declaration of interests

We declare no competing interests.

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