Review

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Review

A Call for Global Transition from Oral Polio Vaccine to Inactivated Poliovirus Vaccine

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Abstract

Background The Global Polio Eradication Initiative (GPEI) is facing two formidable obstacles. Wild poliovirus (WPV) type 1 continues to cause polio in Afghanistan and Pakistan, where, in 2024, there were 93 cases, despite some children receiving over 15 doses of Oral Polio Vaccine (OPV), highlighting suboptimal vaccine efficacy (VE). Genetic variants of vaccine polioviruses viz., circulating vaccine-derived polioviruses (cVDPVs), continue to cause polio. In 2024, there were 253 cases in these same two countries, Afghanistan and Pakistan, highlighting OPV's serious safety problem. No other childhood vaccine has such a bleak record. **Methods** We analysed annual numbers of polio reported by the GPEI during 2008-2024. GPEI does not permit public access to the annual numbers of vaccine-associated paralytic polio (VAPP) cases, polio caused by non-circulating vaccine-derived poliovirus known as ambiguous VDPV (aVDPV) and polio due to immunodeficiency-related VDPV (iVDPV). Therefore, we have estimated their numbers based on a review of publications that counted cases for research purposes; we then extrapolated to arrive at a global figure. **Results** Globally the number of iatrogenic polio cases surpassed that of WPV polio in 2012 and cVDPV polio alone surpassed that of WPV polio in 2017. In the last 7 years (2018-2024), the total of 489 WPV cases and 3,955 cVDPV cases show that there were eight cVDPV polio cases for every case of WPV polio. With the estimated total of 4347 cases of iatrogenic polio (VAPP, iVDPV, aVDPV and cVDPV cases), the ratio is nearly nine cases caused by vaccine polioviruses and their variants for every case of WPV polio. **Conclusion** The continued use of OPV is associated with an approximate nine-fold increased risk of iatrogenic polio in comparison with endemic WPV-1 polio, during 2018-2024. Therefore, its continued use is unjustified because of sub-optimal VE and serious safety problems. Risk-free protection from polio can be provided with use of inactivated poliovirus vaccine (IPV) which has near-100% VE for three doses. Giving IPV under the Expanded Programme on Immunization, followed by the discontinuation of OPV, is the right way forward to achieve and sustain polio eradication globally.

Keywords: global polio eradication initiative; iatrogenic polio; vaccine efficacy; vaccine-derived poliovirus; wild poliovirus

Introduction

The World Health Assembly (WHA) resolved in 1988 to eradicate polio by 2000, assigning the task to the World Health Organisation (WHO) and recommending that it be achieved through the Expanded Programme on Immunization (EPI) [1]. The resolution emphasized that eradication efforts should be pursued in ways that strengthen EPI, while improving disease surveillance and laboratory diagnosis of polio [1]. Despite global expert opinion for using the Salk inactivated poliovirus vaccine (IPV) that was already available as quadrivalent vaccine combining IPV and diphtheria-pertussis-tetanus antigens [2], EPI chose to continue exclusively with oral polio vaccine (OPV), which had been

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introduced into EPI a decade earlier for its low cost and ease of administration [2]. In fact, the quadrivalent vaccine was even easier to incorporate within EPI than OPV, since no added time or effort was required for vaccination and extra space in the cold chain would be avoided. The cost of the quadrivalent vaccine was higher than the costs of OPV plus DTP. However, the overall cost might have been lower with IPV than with OPV for several reasons: only 3 doses of IPV suffice for 100% VE; absence of vaccine-associated paralytic polio (VAPP) to be tested, treated and rehabilitated; and reliance on repeated supplementary vaccination campaigns would have been avoided.

Despite raising the bar from merely immunising against polio under the EPI to eradicating polio as resolved by the WHA in 1988, the EPI immunisation strategy was not revised until late in the 1990s, when supplementary campaigns using OPV were added, without adoption of IPV.

To reiterate, IPV was completely safe with exquisitely high vaccine efficacy (VE), while OPV had the occasional serious adverse event following immunisation (AEFI) by way of VAPP and the frequent 'primary vaccine failure polio' in children who had swallowed 3 or 4 doses of OPV [3–5]. In contrast, no child had been reported to develop polio after taking 3 doses of IPV.

As the EPI could not eradicate polio by 2000, a special governing structure called the Global Polio Eradication Initiative (GPEI) was established which unfortunately did not re-examine the best way to eradicate polio in light of the failure, other than to accelerate reliance on mass OPV campaigns. GPEI did not coordinate with EPI to change the policy from OPV to IPV.

The incorrect path chosen for global polio eradication resulted in two failures: (1) WPV type 1 has still not been eradicated 25 years past the target date, despite expenditures by GPEI of approximately one billion US dollars annually with consequent diversion of host country human and financial resources; and (2) polio outbreaks have been recurring, caused by vaccine viruses reverting genetically to circulating vaccine-derived polioviruses (cVDPV) types 1, 2 and 3 [6].

The purpose of this paper is to review the consequences of not taking the right path and to propose a relatively easy and practical way to take the right path in order to rapidly complete polio eradication.

Methods

We reviewed data published by WHO and the U.S. Centers for Disease Control and Prevention (CDC) to collect annual case numbers of WPV polio and cVDPV polio from 2008 through 2024 [7–10].

VAPP has been known for a long time as a serious adverse event following OPV vaccination due to its residual neurovirulence [11,12]. However, VAPP cases are not publicly reported by GPEI. More than 10 years ago, VAPP cases following use of trivalent OPV was estimated to be 306 to 490 cases annually, which was projected to decline by 80-90% after administration of one dose of IPV [12]. It was estimated that VAPP cases would decline by 90% by the withdrawal of type 2 and introduction of a single dose of IPV under the global switch from trivalent to bivalent OPV. For the year 2016 due to the global switch to a single dose of IPV, we have assumed a modest reduction of 50% in VAPP cases and thereafter of 90%. That would result in roughly 40 VAPP cases per year for the past decade.

Immunodeficiency-associated vaccine-derived poliovirus (iVDPV) causes polio in individuals with primary B-cell immunodeficiency disorders. Ambiguous vaccine-derived polioviruses (aVDPV) is VDPV that is neither iVDPV nor cVDPV. The annual figures were estimated from the sources available from CDC [13–18].

Results

Vaccine polioviruses and iVDPV, aVDPV and cVDPV cause polio at varying frequencies. VAPP, as well as polio due to iVDPVand aVDPV, occur sporadically; cVDPV causes polio outbreaks (viz. 2 or more cases). The annual numbers of polio cases caused by WPV and cVDPV as reported by GPEI, and the estimated numbers of polio cases caused by OPV (viz. VAPP, aVDPV and iVDPV) during 2008 to 2024 are presented in the Figure 1.

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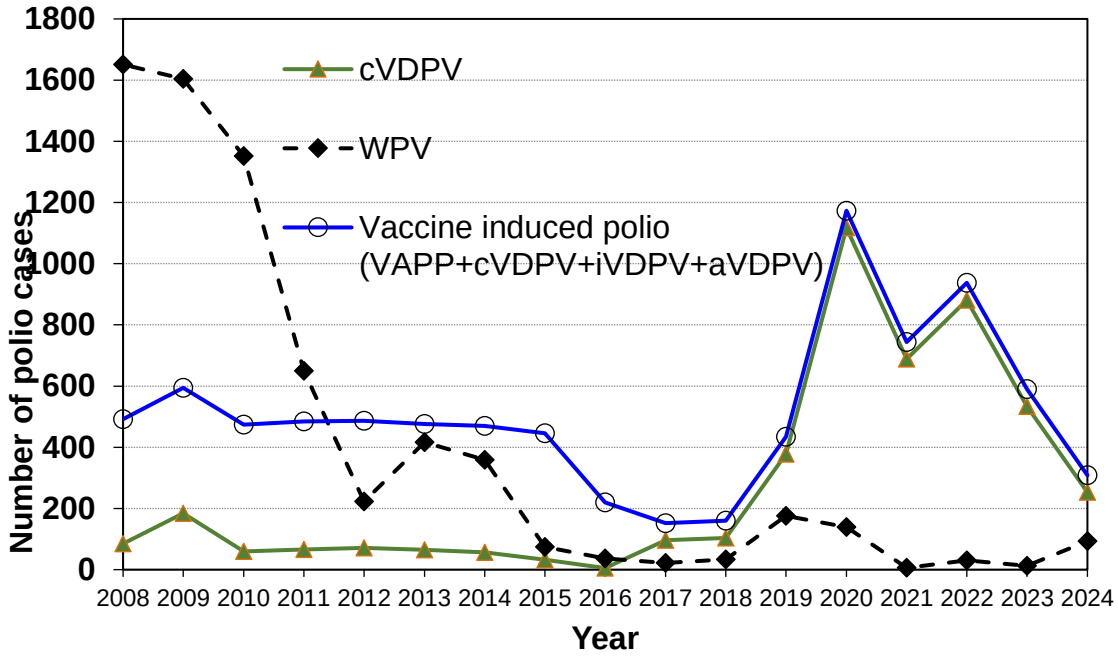

Figure 1. Time trend of annual numbers of reported polio cases due to WPV and cVDPV and estimated numbers of all iatrogenic polio cases (VAPP and polio cases due to aVDPV, iVDPV and cVDPV) during 2008-2024. From 2012 until 2024, the annual numbers of iatrogenic polio cases have exceeded those from wild poliovirus.

There was a steep reduction in WPV cases during 2008-2012. On the other hand, polio cases due to cVDPV increased steeply during 2018-2020.

There was a decline of all-cause polio during 2020 with a small rise again later. The annual number of iatrogenic polio cases surpassed that of WPV in 2012 and has stayed so thereafter. The number of cVDPV polio surpassed that of WPV polio in 2017 and has stayed so thereafter.

In the last 7 years (2018-2024), with a total of 489 WPV cases and 3955 cVDPV cases, eight cVDPV cases of polio occurred for every case of polio caused by WPV.

The difference between WPV-polio and vaccine-induced polio cases becomes more striking with the blue line representing all estimated vaccine-induced cases of polio (cVDPV, VAPP, iVDPV and aVDPV). The ratio increased to 8.8 cases caused by vaccine-derived polioviruses for every WPV polio case.

Discussion

GPEI clearly lost its way towards polio eradication from its inception. The negative consequences of avoiding the right path have been enormous. In 2008, eight years after the target year for polio eradication, there were over 1600 cases of WPV polio. It was widely known that no country that used only IPV in national childhood immunisation programme, or switched to IPV from OPV, had any polio, wild or iatrogenic, while the continued problem was only in OPV-using countries under the GPEI strategy. It was also widely known that the reason for the delay in eradication of WPV polio using OPV was the low VE of OPV, particularly types 1 and 3. Strangely, the failed polio eradication programme became the new normal. Instead of taking the right path, the GPEI partnership and their donors like Rotary International, UNICEF, the Bill and Melinda Gates foundation, Gavi (the Vaccine Alliance) and the US Centers for Disease Control and Prevention (CDC) showed no urgency to find the right path. Polio caused by VDPVs – iVDPV, aVDPV and cVDPV –appeared in many countries using OPV from 2000 onwards. Yet, the casual connection between the vaccine in use in those countries seems to have been ignored. Iatrogenic polio surpassed natural polio in 2012, by which time the new normal was accepted by the programme leadership and partners.

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Among the vaccine virus variants, cVDPV is the most dangerous as it causes polio outbreaks. Among the three antigenic types, cVDPV-2 was known for its persistence in communities, signalling that it behaved closer to WPV than to cVDPV types 1 and 3. Yet, type 2 vaccine virus was not withdrawn from trivalent OPV at the appropriate time; the delay led to cVDPV-2 capturing the niche vacated by WPV-2.

During 2020-2021, both WPV and cVDPV-2 showed a sharp decline. The COVID-19 pandemic began in early 2020 and despite disruptions in immunisation activities, polio incidence declined. Since WPV and cVDPV are both respiratory-transmitted (see later), the fall in polio cases can be explained by the reduced social contacts and the wearing of face masks by adults and adolescents.

In 2022 during the COVID-19 pandemic, there was a second peak in reported polio cases, presumably due to resumption of normal life. Thereafter, the continued decline was probably due to the widespread use in catch-up campaigns of novel OPV (nOPV), a genetically engineered live vaccine designed for reduced neurovirulence, thereby resulting in a four-fold reduction in cVDPV [19].

All the above vaccine-derived polioviruses cause paralysis that is clinically indistinguishable from wild poliovirus. While these various definitions are useful for epidemiological surveillance, they make no difference in the suffering of the victim paralysed by the virus.

In 2024, there were 93 cases of WPV polio but 253 polio cases (2.5 times more) due to cVDPVs alone [20]. Also in 2024, more than nine times as many countries reported cVDPV cases than WPV polio (19 versus 2).

Since the low cost and ease of administration of OPV were not valid reasons for the exclusive use of OPV, polio experts argued that OPV was essential to eradicate WPVs on account of the local intestinal mucosal immunity induced by it [21]. The purported evidence was that OPV-induced immunity reduced the duration of vaccine virus shedding when challenged with repeated doses of OPV, as compared to IPV-induced immunity. Unexplained was why, in the first place, a child immunised with OPV would shed virus at all, when given a subsequent dose. If OPV-vaccinated children were susceptible for repeat infection by vaccine viruses themselves, they would surely also be susceptible to ‘re-infection’ when exposed to WPVs. The logical interpretation of vaccine virus re-infection should have been that polioviruses cause re-infection despite humoral and local mucosal immunity. Indeed, we have shown that local intestinal mucosal immunity is unimportant for polio eradication [22].

Furthermore, the importance attributed to intestinal immunity was contingent upon an unproven assumption that the transmission route of WPV was faecal-oral [23]. It was not supported by any research or evidence. The very age-distribution of polio in lower and middle-income countries (LMICs) that was skewed dramatically to the left, even more so than that of measles, flies in the face of this assumption. It turns out that the route of transmission is respiratory, sourced from re-infected older children and/or adults [24–26].

In real life situations, OPV was not highly efficacious in LMICs in the tropical zone, proved by the relatively high frequency of primary vaccine-failure polio. Three doses of OPV fail to induce systemic (humoral) immunity in over 70 per cent of children in North India [27]. Yet, cVDPVs cause polio outbreaks in tropical LMICs. Vaccine viruses are inefficient to infect after deliberate feeding and not contagious despite successful infection. Yet, cVDPV is highly contagious causing outbreaks. Our interpretation is that cVDPVs acquire transmission efficiency by the respiratory route, while vaccine viruses bypass the upper respiratory region [28].

Conclusion

There is glaring evidence that OPV is an unsafe vaccine and should have been discontinued and IPV universally ramped up before 2000. This delay has resulted in thousands of iatrogenic polio cases, which are no different from wild virus polio cases in terms of immediate and lifelong suffering. Even if the nOPV has contributed to reducing cVDPV, the safety risk is not zero [9,29]. In addition, its use does not improve the efficacy of OPV, which has been poor in tropical LMICs necessitating repeated

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mass campaigns [29]. These campaigns themselves amplify the risk of continued seeding of cVDPVs, which is contrary to the aims of eradication.

The right path forward is to protect children from polio caused by all live viruses, using IPV through routine immunisation. The use of IPV, included in the hexavalent vaccine formulation, in a primary three-dose series during infancy plus a booster in the second year will protect every child everywhere from polio paralysis and help to achieve global eradication faster on account of its herd effect [30].

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