PERSPECTIVE

Global Polio Eradication: The Journey So Far

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The Global Polio Eradication Initiative (GPE I), since its launch in 1988 has achieved more than 99% reduction in polio cases globally, using oral polio vaccine (OPV). Currently only two countries (Pakistan and Afghanistan) have not been able to stop transmission of wild poliovirus (wPV). In this article, we discuss some of the challenges faced by these two countries. The lessons learnt from the tremendous public health success stories of India and Nigeria are also highlighted. Reintroduction of wPV in the polio-free areas remains a valid risk globally and some recent examples are discussed. Inactivated polio vaccine (IPV) is the most accepted risk-mitigation strategy to secure a polio-free world from both wPV and circulating vaccine derived poliomyelitis (VDPV). The challenges related to switch from trivalent to bivalent OPV and introduction of IPV in 156 countries using trivalent OPV, are also highlighted.

Keywords: *Afghanistan, Global Polio eradication, India, Nigeria, Pakistan.*

The Global Polio Eradication Initiative (GPEI) is at a historical moment. Since its launch in 1988, the burden of polio cases has come down from an estimated 350,000 cases in 125 endemic countries to 73 cases in two endemic countries, a reduction of more than 99% [1,2]. In 2015, a total of 73 cases caused by wild poliovirus (wPV) were reported from these two countries: Pakistan (*n*=54; 74%) and Afghanistan (*n*=19; 26%) [3,4]. Compared to year 2014, these figures reflect 82% reduction of cases in Pakistan (*n*=306) and 32% for Afghanistan (*n*=28). Nigeria that reported 6 wPV cases in 2014 did not report any fresh cases in 2015 and was removed from the list of polio endemic countries in September 2015 [3,4].

The world has witnessed this tremendous progress using trivalent oral polio vaccine (tOPV) [1]. The use of tOPV has successfully eliminated wild poliovirus type 2 (wPV2), and wild poliovirus type 3 (wPV3), which have not been detected globally since 1999 and November 2012, respectively [1]. Four of the six World Health Organization (WHO) regions have been certified as polio free: the Americas in 1994, the Western Pacific Region in 2000, the European Region in 2002, and the South East Asia Region in March 2014 [2,3]. The four main strategies used to achieve polio elimination are as follows [1].: (*a*) Using tOPV in routine immunization; (*b*) Strengthened polio disease surveillance; (*c*) Supplemental immunization activities (SIAs); and (*d*) Mop-up campaigns in areas with sustained transmission.

POLIO SITUATION IN PAKISTAN

The regions of persistent polio transmission in Pakistan are geographically grouped into four areas [5]. In the north of Pakistan, a few districts of Khyber Pakhtunkhwa (KP), agencies of The Federally Administered Tribal Areas (FATA) are examples of reservoir areas of wPV transmission [5]. Towards south, the other two reservoir areas are located in the provinces of Sindh and Baluchistan. Although the greatest challenge remains in specific small areas, eradication still seems an uphill task [5].

Main reasons behind the huge upsurge in 2014 are claimed to be militancy and 'refusal families' in FATA and KP. However, larger threats to polio campaign in Pakistaninclude program mismanagement, campaign design, poor data quality from the field leading to miscalculation in vaccination coverage estimates, and estimated poor quality of vaccine administered across the country [6].

Pakistan health agencies, other international agencies, and local civil society organizations have taken several steps to strengthen its OPV program. Pakistan has introduced injectable polio vaccine (IPV) in its routine Expanded Program on Immunization (EPI) starting from 20th August 2015 [5]. IPV will benefit more than four million children in Pakistan every year. Frequent movement of Afghan refugees in the bordering areas of FATA and KP already serving as polio reservoirs further complicates the situation [5]. Pakistan and Afghanistan have realized that they need to coordinate intensely in polio eradication drives.

Pakistan has never reported a polio case count as low as in 2015 and till date in 2016. The country is still aiming

at a shift from the trivalent to bivalent OPV, but will not be able to completely withdraw OPV even for years after the target date, thus causing a delay in containment and certification [5, 6]. It is hoped that coordinated activities with partner support will help achieve polio-free status in the near future.

AFGHANISTAN: THE CURRENT SCENARIO

Challenges to interrupting poliovirus transmission in Afghanistan include: limited healthcare infrastructure and personnel, low routine vaccination coverage, high rates of poverty and illiteracy, cultural norms that may restrict caregiver interaction with vaccinators, and subpopulations that travel frequently to border areas of Pakistan, where wPV transmission is endemic [7]. Supplementary immunization activities (SIAs) are hampered by areas of armed conflicts, limited monitoring and evaluation of coverage, and insufficient local program accountability, and effectiveness to reach all children [7].

The frequent cross-border migration of ethnic groups shared with Pakistan requires close coordination of each country's respective immunization efforts [7,8]. At the beginning of 2016, Pakistan and Afghanistan decided to increase micro-synchronization of polio campaigns at the border, closer monitoring of nomadic movement across borders, strengthening of transit vaccination, and holding of synchronized polio campaigns in future [5].

THE SUCCESS STORY OF POLIO ERADICATION IN INDIA AND NIGERIA

A. India

The critical lessons learnt from India's elimination of WPV are as follows [8]:

a) India engaged every level of government and made district administrators lead task forces to review SIA planning and implementation;

b) Developed strong communication strategies;

c) Optimized vaccination team composition by including one male and one female member from local community to facilitate entry into households;

d) Developed and validated microplans in which, all houses in the area were numbered and realistic workloads established for each vaccination team;

e) Real time monitoring of campaign quality and independent coverage assessment at the end of each round;

f) Ensured accountability;

g) Engaged the private sector to increase program visibility and reach maximal impact.

Several innovative strategies, and tactics to identify and vaccinate children who were previously being missed were included [9]:

1. Engaging community and religious leaders in planning and implementing SIAs in areas with reluctant participants;
2. Finger marking of vaccinated children to help identify those not yet vaccinated and marking the dwellings of households visited by vaccination teams to increase the likelihood of follow-up;
3. Identifying and tracking newborns; targeting high-risk areas with multiple health interventions and additional resources;
4. Implementing a strategy for reaching children at public gatherings and in mobile and transitory populations.

India also conducted research to help overcome technical and operational barriers including introduction of more efficacious vaccines (i.e., monovalent OPV in 2005 and bivalent OPV in 2010); seroprevalence and immunogenicity studies and operational studies such as social network analysis to provide evidence for decision-making [9].

B. Nigeria

In 2011-12, Nigeria experienced an upsurge of polio transmission and the country became a net exporter of poliovirus to polio-free countries [8,10]. However, at the end of 2013, the number of cases of wPV type 1 infection had decreased by 58%, with no wPV type 3 transmission [10]. wPV transmission in Nigeria was driven by reservoirs in northern Nigeria [10]. Additionally, three states in the northeast region suffered from increased militancy and security problems and several health-care workers doing polio work were killed [8,10].

Nigeria along with the international partners undertook several programmatic interventions like those described for India [10]. These interventions were enabled by a focused effort to obtain the necessary resources, use them effectively and transparently, provide the needed public health workforce, and ensure accountability for results [8,10]. This resulted in Nigeria being removed from polio endemic list in September 2015 [3,4].

RECENT IMPORTATIONS OF WILD POLIOVIRUS

During 2014, a total of 19/359 (5%) wPV cases were due to outbreaks following importation into previously polio-free countries in Central Africa (Equatorial Guinea and Cameroon), the Horn of Africa (Somalia and Ethiopia),

and the Middle East (Iraq and Syria) [4]. Among these countries, Guinea and Iraq reported imported cases of wPV after remaining polio free for more than a decade [4]. Israel in 2013 detected wPV in environmental samples in two of its cities, which were genetically traced to Pakistan, however a massive public health campaign prevented occurrence of clinical cases [11]. Thus, as long as wPV circulates anywhere in the world, all countries are at a risk of reintroduction and also at risk for epidemics arising from such imported WPV.

RISKS OF CONTINUED USE OF OPV

Polioviruses contained in OPV (Sabin viruses) are live attenuated, which on rare occasions can revert to neurovirulence and cause vaccine-associated paralytic poliomyelitis (VAPP), clinically indistinguishable from paralytic poliomyelitis caused by wPVs [12-14]. It is estimated that each year between 250 and 500 cases of VAPP occur worldwide [1]. The number of VAPP cases far exceeded the number of wPV cases since 2012, which was ethically unacceptable and thus, led to change in strategy of polio end game.

In addition to causing VAPP, Sabin viruses may mutate and subsequently gain the ability to circulate in communities for long periods of time; these are referred to as vaccine-derived polioviruses (VDPVs) [1]. VDPVs would have also lost their attenuating mutations and therefore re-acquired both the neurovirulence and transmission characteristics of wPVs [1]. On very rare occasions, VDPVs could potentially re-establish endemic and epidemic transmission, leading to polio outbreaks from these circulating vaccine derived polioviruses (cVDPVs), and they are therefore incompatible with polio eradication [1].

Over the past decade, more than 40% of VAPP and 90% of the cVDPV cases have been caused due to the type 2 polio component contained in tOPV [15]. In 2015, 29 cases of cVDPs were reported globally with most (n=26) from non-endemic countries and two from Pakistan [4]. Since wPV2 hasn't been reported since1999, the risks of delivering OPV2 outweigh the benefits.

IPV- A RISK MITIGATION STRATEGY

To secure a polio free world from both wPV and cVDPs, the GPEI's "Polio Eradication and Endgame Strategic Plan (PEESP) 2013-18" has introduced IPV alongside the OPV [14]. Since the last natural case caused by poliovirus type 2 occurred in 1999 and the poliovirus type 2 causes most cases of VAPP and cVDPs as explained previously, removal of poliovirus type 2, from the current tOPV is the most logical next step in PEESP 2013-18 [14]. Using a bivalent OPV (bOPV), containing Sabin poliovirus type 1 and 3 without type 2 virus has started in April 2016. This will be followed by withdrawal of all OPV in 2019-20 [14]. Since, bOPV has higher immunogenicity per dose [16], seroconversion rates against type 1 and type 3 will improve and further generation of type 2 cVDP will stop [17]. However, bOPV use alone is associated with some risk of type 2 outbreaks in low coverage populations with low immunity against type 2 viruses [17]. The source for such outbreaks can be tOPV if the world is using both trivalent and bivalent OPV at the same time, leading to new type 2 cVDPs [17]. Persistant cVDPs defined as cVDPs circulating for more than 6 months can occur in normal or in immunocompromised patients (iVDPs) [1, 14]. Outbreaks due to breach in laboratory containment of type 2 virus can be another source, as happened in India in 2002 and 2003 [18]. In view of the above-mentioned risks due to switch to bivalent vaccine the PEESP 2013-18 recommends global introduction of at least one dose of IPV into every country's routine immunization schedule [14]. All 156 countries using tOPV are supposed to introduce IPV prior to the switch from 17th April to 1st May 2016 [14].

GLOBAL IPV SHORTAGE AND ITS CONSEQUENCES

There is global shortage of IPV vaccine because of technical failure to scale up vaccine production by manufacturers. The Indian Expert Advisory Group (IEAG) [19] and the WHO [20] have now advocated two fractional doses of IPV (f IPV) in routine immunization for countries facing vaccine shortages, as a risk mitigation strategy to extend coverage. The recommendation is based on two studies, one from Cuba [21] and other from Bangladesh [22]. The study from Bangladesh demonstrated a seroconversion rate of 81% to type 2 poliovirus after two doses of f IPV (0.1mL intradermal) given at 6 and 14 weeks of age [22]. This "prime boost" effect is better than that given by single, full dose (0.5 mL intramuscular). The IEAG also recommended not changing the switch date in India despite global IPV shortage [21]. India has rolled out IPV in all its states prior to the switch date. Seven high performing states Maharashtra, Odisha, Karnataka, Tamilnadu, Telengana, Andra Pradesh and Kerala will follow the fIPV schedule [19].

CHALLENGES IN SWITCH FROM TOPV TO BOPV AND INTRODUCTION OF F IPV

Some challenges for a successful switch are: withdrawal and destroying of tOPV stock; adherence to national guidelines for disposal of tOPV; validation of switch in a short time of three months by independent validation

committee; prevention of accidental or intentional tOPV spread from containment sites. Some of the operational challenges for IPV introduction include: re-training of healthcare staff at all levels of health-care; changes in the operational guidelines; change in communication strategy; changes in the immunization card; assessing the new IPV schedule and delivery of IPV vaccine using BCG syringe in India, role of other formulations of IPV like the Sabin IPV.

Contributors: NT, VNY and AP conceived and planned the review. AP drafted the initial version of the manuscript and revised it with inputs from NT and VNY. All authors critically reviewed the manuscript and approved the final version.
Funding: None; *Competing interest*: NT is GAVI Board member representing civil society organizations and AP is special advisor to NT.

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