Path to Polio Eradication in India: A Major Milestone

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Global polio eradication initiative (GPEI) is arguably the most ambitious and expensive public health project undertaken by the World Health Organization (WHO). The goal set in 1988 by the all-nation World Health Assembly was to achieve eradication of wild polioviruses (WPVs) by the year 2000 [1]. All but 6 countries - India, Pakistan, Egypt, Afghanistan, Nigeria and Niger, achieved elimination of WPVs by 2000 [2]. Later Egypt and Niger also succeeded, leaving 4 countries with endemic WPV transmission beyond 2005 [3]. This delay was not only embarrassing to the countries but also a subject of debate, with some global public health experts expressing doubts on the achievability of the goal [4,5]. The silver lining on the dark cloud of GPEI's woes was that one of the 3 types of WPV, type 2, was eradicated by 1999 [6]. To the optimists that held promise that other types could also be eradicated, but for the skeptics that was signal for the world to be prepared to accept failure and settle for permanent control of WPV types 1 and 3, not eradication [4, 5].

GPEI's ride beyond 2005 was indeed very bumpy. In spite of extraordinary efforts WPV-1 and 3 refused to yield in the 4 countries, mockingly called PAIN (Pakistan, Afghanistan, India and Nigeria). During the last decade some 40 countries that had once interrupted endemic transmission of WPV-1 and 3 experienced re-introduction by importation of either type [3]. A few such instances resulted in large scale outbreaks [7,8]. Interrupting transmission in countries with re-introduction was a heavy burden on GPEI in terms of distraction, funds and vaccine. In 2010, the world witnessed the sea-saw battle without any decisive victory. In 2011 India has changed that gloomy picture by achieving a major milestone: no WPV-3 detected in 2011 and no WPV-1 beyond January [9]. In January 2012 India has crossed one full year without any WPV detection in spite of intensive search through high quality surveillance. WPV-3 has not been found anywhere for 15 months. Uttar Pradesh (UP) has remained without WPV for 20 months and Bihar for 15 months; these 2 states were perhaps the most difficult areas to interrupt transmission of WPV-1 and 3 in the whole world, on account of very high force of transmission and very low vaccine efficacy of trivalent oral polio vaccine (tOPV). India's achievement is indeed a shot in the arm of GPEI and a sign of hope that globally eradication is achievable.

IS THE SUCCESS REAL?

We have been WPV-free for just one year. Technically, absence of WPV for 3 years in the face of sustained high quality surveillance is necessary for global acceptance of elimination. India's surveillance is of exemplary quality. An important piece of evidence that transmission has been interrupted is from investigation of sewage; samples are periodically tested in 3 cities – Mumbai, Delhi and Patna and throughout 2011 they have tested negative for WPVs. Earlier, sewage in Mumbai and Delhi had repeatedly signaled silent WPV transmission, presumably due to virus importation through migrants from UP and Bihar.

Supporting evidence is improved antibody prevalence in infants, measured through serological surveys in districts of western UP and central Bihar, in the last three years. In an unpublished study of the National Polio Surveillance Project (NPSP) in 1280 infants of 6-7 months, in high-risk districts of Uttar Pradesh (UP) and Bihar, prevalence of antibody against types 1 and 3 in 2010 was 98% and 77%, respectively. The corresponding figures in 2008 were 96.5% and 42.6%, and 99% and 49% in 2009. Finally, the number of 'polio compatible cases', which may include some children with true polio but without virological confirmation, was the lowest ever in 2011.

The above set of evidences gives us cautious optimism that the transmission of WPV- 3 and 1 has been interrupted in India in 2010/11. This is indeed a major milestone in our progress towards polio eradication.

WPV type 2 was last seen in 1999 – its eradication was the first milestone.

HOW DID WE ACHIEVE SUCCESS?

Several agencies contributed to this success – GPEI, NPSP, Immunization Division of the Ministry of Health, UP and Bihar State Governments, district administrative and health personnel, health workers and families themselves. Several factors contributed to this success. First, sustained intensive vaccination in successive waves of pulses, as often as 10 per year, sustained over 6 consecutive years – something no other country has done or would perhaps be capable of doing. Second, the diligent steps in finding and vaccinating children of families in their millions who migrate within and outside home State for unskilled employment. Third, the use of monovalent and bivalent OPVs. Since 2005 these were investigated for confirming superiority of efficacy of mOPV-1 and 3 over that of trivalent OPV (tOPV) and the non-inferiority of bivalent OPV (bOPV, types 1 and 3) against mOPVs [10, 11]. The documentation of sustained near-100% antibody prevalence against type 1 in infants and rising prevalence of antibody against type 3 with the use of the new OPVs in supplementary vaccinations in the high risk regions made credible the success of the new interventions.

Western UP and central Bihar were the two 'hotspots' as far as endemic polio in the country was concerned, during the last decade. Vaccine failure due to very low vaccine efficacy of tOPV and failure to vaccinate all young children (leaving sufficient numbers to continue virus circulation) contributed to the long delay before achieving success. With the introduction of mOPV-1 from 2005 and of bOPV from December 2009, immunity gaps reduced. Modified strategy with focus on hard-to-reach districts and blocks and vaccination of migratory population did remarkably well. The national tally of polio due to WPVs declined to 42 scattered in 17 districts during 2010, in contrast to previous three years, with numbers of 559 to 874 cases in 56 to 99 districts. UP and Bihar became free of WPVs from early or mid-2010; the last case of WPV polio in January 2011 was not in UP or Bihar, but in Howrah district of West Bengal. Intense vaccination efforts stopped its transmission quickly.

THE RISKS AND THREATS FACING INDIA

Three risks have to be borne in mind to guide India's future actions. Complacency will be dangerous since we have not passed the three-year polio-free period to be absolutely certain of the absence of unrecognized silent WPV transmission somewhere that might show up sometime within that interval. Thus the first risk is of silent transmission of WPV that has eluded detection. The WPV detected in Howrah in January 2011 was closely related to the WPV found in Delhi sewage 5 months earlier, but in that interval that genetic lineage virus was not detected anywhere else. Virus without progenitor genotype detected within one year is called 'orphan' virus. In central Bihar 'orphan' virus (WPV 1) was detected in 2009 [12] which subsequently circulated during the rest of the year. Another risk of undetected WPV circulation could be in migrant, mobile, and underserved communities. Most WPV isolates in India in 2010 were those detected in previously polio-free areas, obviously imported from UP or Bihar. The NPSP has several examples of virus appearing in migrant or underserved communities in high risk areas, for example in Malegaon, Maharashtra in 2010 and Howrah in West Bengal in January 2011 [12].

While WPV-3 has remained in silent transmission for one year in the past in some countries and showed up later, such a situation is unlikely in 2011/12 for 2 reasons. The currently used vaccine for local supplementary vaccination campaigns in the traditional high risk areas of UP and Bihar is bOPV. Its type-specific efficacy to type 3 (and to type 1) is 2-3 times higher than that of tOPV. Bihar and UP had high prevalence of WPV-3 during 2007-2009, but very low transmission in 2010, and have remained without infection since then. WPV-1 on the other hand had not remained undetected in silent transmission for one year any time in the past where surveillance was efficient.

The second risk is re-introduction of WPV into India from countries that have not yet eliminated transmission or had been re-infected after elimination. Pakistan, Afghanistan and Nigeria have remained without ever having eliminated WPV 1 or 3. Currently several countries in Africa have WPV 1 or 3 due to importation from elsewhere. In 2011 WPV-1 from Pakistan was introduced in China where several cases occurred before its transmission was stopped [13]. With the recognized potential of adults acting as vehicles of virus importation, India has to remain vigilant and cannot reduce the intensity of surveillance. If WPV is detected anywhere, immediate mop up using the relevant mOPV type must be applied to contain and eliminate it. High vaccination coverages in the Universal Immunization Program (UIP) and during annual pulse immunization are essential to keep up childhood population immunity at the highest possible levels in order to prevent the spread of any imported WPV.

The third risk is continuing occurrence of polio as the inevitable aftermath of the use of OPVs to get rid of WPVs. Vaccine-associated paralytic poliomyelitis (VAPP) is unavoidable as long as OPV is in use. The Ministry of Health, Government of India, does not count VAPP as polio with the justification that VAPP is sporadic and poses little or no threat to others. Thus it is epidemiologically irrelevant, while ethically remaining problematic. This position is not completely satisfactory, but we hope that one day soon we can stop using OPVs altogether and stop causing VAPP in any child. Vaccine-derived polioviruses (VDPVs) are a greater threat to polio eradication itself. Vaccine viruses are transmissible and genetically unstable, with a tendency to revert genotypically and phenotypically to become increasingly wild-like. Any virus isolate that is of vaccine virus lineage and had shown sufficient genetic deviation from the original vaccine virus to show its continued replication in human intestine for more than 6 months, is called VDPV. It causes polio and tends to spread rather like WPV. When one genotype of VDPV is found in at least 2 children with polio, we know that it has circulated very widely – and is called circulating VDPV (cVDPV). If allowed to evolve, it can circulate like WPVs, thus negating the very eradication of polio. Thus any case of paralysis due to VDPV is counted as polio. Even though polio due to VDPV does not negate the success of eliminating WPVs, its presence is epidemiologically risky as it can spread widely in the community. Fortunately, rather due to the very high immunity prevalence established by the extraordinary measures described above, there has been only very few VDPV polio cases in recent years – 21 in 2009, 5 in 2010 and 6 in 2011 [14]. Further emergence of VDPVs must be preempted in future and if that fails then intercepted and eliminated before it spreads widely into new geographic areas [15]. These can only be achieved if the non-infectious inactivated poliovirus vaccine (IPV) is introduced in UIP, very high (~90%) coverage achieved and then OPV is withdrawn from use [16]. These are challenges facing India as we celebrate the interruption of WPV transmission in India.

END GAME STRATEGY

The programme activities in the immediate post-WPV eradication phase when the risk of VDPV remains are generally referred to as 'end game' of GPEI. Globally a firm strategy for the end game has not been finalized. Options are currently being discussed and debated. True polio eradication will be achieved only after the end game [17]. Therefore the strategy for end game must be carefully crafted and approved by the World Health Assembly.

The earlier belief that OPV could be withdrawn by any country if it so wishes after eradicating WPVs globally was flawed and no one subscribes to it any more [15]. Fearing the emergence or cross-border transmission of VDPVs with asynchronous withdrawal of OPV, the idea of globally synchronized cessation of OPV emerged [18]. One line of thinking currently under consideration of GPEI is globally synchronized withdrawal of type 2 in OPV; in other words to replace the global supply of tOPV with bOPV. We are not in favor of this move as it may result in cVDPV-2 spreading widely, in which case tOPV will have to be re-introduced. Such an eventuality may undermine the trust nations have in GPEI. The obstinate recurrence of cVDPVs in different countries in recent years has led to wider acceptance of the precept that it will be wiser to introduce IPV to establish high immunity prevalence as a pre-condition for cessation of OPV (16).

At present IPV is unaffordably expensive for low income countries. The GPEI had been exploring ways to reduce the cost of IPV. One approach that has been tested is to give it intradermally in fractional dose [19-22]. In one recent Indian investigation [23], IPV given intradermally via a needle-less device was found to be less immunogenic than what has been documented with injected vaccine in both early studies in India and recent studies elsewhere [19-22]. Traditionally IPV has no adjuvant. Reducing antigen while retaining immunogencity if IPV is adjuvanted is under exploration.

Currently available IPV is made from inactivating laboratory-maintained fully virulent WPVs. In a polio-free world, keeping WPVs in any vaccine manufacturing facility is fraught with risks of inadvertent leak. Therefore studies are ongoing in several places to make IPV using Sabin virus strains; even if accidental leak occurs, the repercussions will be less ominous than from virulent viruses.

FUTURE PERSPECTIVES

The Government has to be prepared to introduce IPV and achieve high coverage after the elimination of WPVs in India. Since WPVs have in all probability been interrupted in 2011, the introduction of IPV should be latest by 2014/15. Careful design of the sequence of use of IPV and withdrawal of OPV is essential and urgent in order to avoid VAPP and to assure complete safety from the emergence or spread of cVDPVs. Clinical and virological surveillance for poliovirus will have to be sustained for several more years when IPV is introduced and continued after OPV is withdrawn so that any

cVDPV will be detected at the earliest. In case cVDPV is found, its elimination must be achieved with IPV since re-introduction of OPV will be most unwise.

As we recall that on an average 500-1000 children were getting polio paralysis every day in the 1970s and 1980s, the day is fast approaching when India can assure all children that not even one would develop polio after the end game of polio eradication is successfully managed.

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