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“Since 2004, the number of wild poliovirus cases confirmed per year has remained above 1000 and since 2006, the number of countries that have never interrupted transmission of poliovirus has remained unchanged at four...”

After the World Health Assembly resolved in 1988 to eradicate wild poliovirus (WPV) transmission globally by 2000, dramatic progress in reducing polio cases and increasing the number of countries that interrupted indigenous WPV transmission was made by 2000 [1]. In 2010, 10 years past the target date and with US\$7 billion of external funds expended since the beginning of the effort, some individuals question the feasibility of reaching the goal [2,3]. This editorial will provide an overview of the polio eradication strategies, progress to date, challenges and efforts to overcome those challenges that, although substantial, are surmountable.

Polio eradication strategies

Four key strategies have been used to interrupt transmission of WPV in nearly all countries of the world [4]:

- Strengthening routine childhood immunization with the oral poliovirus vaccine (OPV);
- Conducting supplementary immunization activities (SIAs), mass campaigns to provide additional doses of OPV to all children under 5 years of age;
- Conducting surveillance for WPV through investigation of acute flaccid paralysis (AFP) cases among children under 15 years of age, and laboratory characterization of polioviruses isolated from stool specimens;
- Conducting intensive house-to-house targeted ‘mop-up’ campaigns in focal areas surrounding recently identified polio cases.

Paralytic disease occurs in less than 1% of WPV infection with one of three serotypes. Live-attenuated OPV is the vaccine of choice for the eradication effort owing to its ease of administration, low cost, secondary immunization of close contacts and better intestinal immunity than the injectable, inactivated poliovirus vaccine (IPV). In tropical developing countries, OPV has lower immunogenicity compared with industrialized countries. Diarrhea, competing infections with nonpolio enteroviruses and other polio serotypes in the standard trivalent OPV (tOPV), and higher levels of maternal poliovirus antibody are risk factors for reduced serologic response [5]. Lower seroconversion rates per dose can be overcome with additional doses, but can require multiple doses to reach the high population immunity levels needed to interrupt transmission. Use of OPV is complicated by the rare outcomes of vaccine-associated paralytic polio, chronic shedding of revertant poliovirus by B-cell-immunodeficient individuals and the emergence of circulating vaccine-derived polioviruses (cVDPV), which are biologically equivalent to WPV, in some populations with low routine immunization coverage [1,6]. Owing to these complications, use of OPV use must cease globally and in a coordinated fashion once WPV transmission has been interrupted [6,7].

Current status of polio eradication efforts

Since 1988, global polio incidence has declined by more than 99%, from an estimated 350,000 cases in 125 countries to

1606 confirmed cases in 2009 [101]. Circulation of WPV type 2 was interrupted globally in 1999 owing to the superior immunogenicity of the type 2 component of tOPV [1,4,5]. Although substantial progress was made before 2000, the pace of progress stagnated in the following decade. Since 2004, the number of WPV cases confirmed per year has remained above 1000 and since 2006, the number of countries that have never interrupted transmission of poliovirus has remained unchanged at four: Pakistan, Afghanistan, India and Nigeria. In each of these countries, health systems are weak and routine immunization coverage is low in the areas where WPV transmission persists. To accelerate eradication, monovalent OPVs (mOPVs) against types 1 and 3 were developed and introduced in 2005, after serotype-specific seroconversion in children was found to be 1.5–3-times more effective per dose than tOPV [8,9]. In nontemperate climates, median seroconversion was 81% after a single mOPV1 dose and 72% after a single mOPV3 dose, compared with 78 and 62% reported after two tOPV doses, respectively [10,11]. Preferential use of mOPV1 to eliminate WPV type 1 has not interrupted transmission globally; in the meantime, accumulated susceptibility allowed outbreaks of type 3 to occur, which replaced reductions in type 1 cases [1,101]. A bivalent OPV (bOPV) formulation was recently developed that provides superior immunogenicity against both types 1 and 3 compared with tOPV and was found to be noninferior to the mOPVs of each serotype after two doses [12]. bOPV was used first in December 2009, and has been scaled up in 2010 for use in most SIAs.

Two major waves of international spread of WPV occurred during 2003–2009, with India and Nigeria serving as the originating WPV reservoirs for outbreaks in countries that were once polio free [1,13,14]. In 2009, 23 countries reported WPV cases, including: the four countries that have never interrupted WPV transmission; four countries with re-established WPV transmission (circulation proven or suspected to persist for >12 months), following WPV importation before 2009, (Angola, Chad, the Democratic Republic of the Congo [DRC] and South Sudan); and 15 countries in Western and Central Africa, and the Horn of Africa, which had WPV cases due to new importations during 2009 [14,101].

Reasons for continuing WPV transmission

Failure to vaccinate

For most countries in which WPV continues to circulate, including African countries, Afghanistan and Pakistan, failure to achieve optimal OPV coverage both in routine immunization programs and during SIAs is the primary problem. Failure to vaccinate has been a particular problem in northern Nigeria, which has never interrupted transmission and was the WPV source for 16 of the 19 other countries in Africa that reported polio during 2009 [14,15,101]. For example, 182 (47%) of the 388 children with WPV cases during 2009 had received less than three OPV doses and population estimates in 12 northern Nigerian states indicated that approximately 30% of children had received less than three doses, although this is an improvement from past years.

However, a turning point occurred in 2009 with improvements in immunization delivery owing to improved federal and state government commitment and leadership, involvement of traditional

and religious leaders, and increased international assistance. During the second half of 2009, dramatic decreases in confirmed WPV cases and control of a multiyear type 2 cVDPV outbreak occurred [15,101]. As of 5 April 2010, major areas of the north have been without WPV cases since July 2009 and only three WPV cases have been confirmed in the country since 1 November 2009. Since more than 20% of children remain unvaccinated in some areas of the northern states of Nigeria, there are concerns regarding whether decreasing trends in cases can be sustained unless further gains are made in coverage. Failure to vaccinate is also the major reason for ongoing polio transmission in outbreak countries in Africa [14,101].

In Afghanistan and border areas of Pakistan, serious security problems and isolated populations have limited access to vaccinate children and have been extremely challenging to address. Local negotiations with political and tribal leaders have provided intermittent opportunities to reach higher proportions of children. However, substantial transmission also occurs in accessible areas of Pakistan because of low routine and SIA coverage due to administrative and management deficiencies [16].

Among the four countries with re-established transmission, civil unrest in Chad, South Sudan and DRC has prevented high routine and SIA vaccine coverage. WPV transmission was interrupted in Angola from 2001–2004 despite a long civil war, but transmission after multiple WPV importations from India since 2005 did not stop because of weak routine and SIA coverage [14]. As in Nigeria, confirmed WPV cases have declined in Angola, South Sudan and DRC during the second half of 2009 after SIA supervision, monitoring of quality and international support were intensified [101].

Vaccine failure

In India, WPV transmission has persisted only in areas of two northern states in 2009; both of these areas have eliminated WPV transmission at some point in time, but not simultaneously [1,17]. OPV effectiveness appears to be particularly low in these areas; among children with WPV cases, greater than 85% received more than seven OPV doses and less than 2% had received fewer than three OPV doses in 2009. Although failure to vaccinate was previously a problem in these transmission areas, by meticulous planning and careful, labor-intensive implementation, coverage in SIAs has reached 99% of the under-5-year-old target population and, recently, greater than 95% of very high-risk migrant and isolated populations. Aggressive efforts to vaccinate the most vulnerable migrant and isolated populations in these and other states with bOPV are planned for 2010; however, it is not known whether this approach will lead to simultaneous interruption of both WPV types 1 and 3 in all areas. Research is essential to identify additional tools and strategies to ensure success. In addition, the government and partners are increasing efforts to improve water quality, sanitation and hygiene in the transmission areas to help diminish the force of infection.

Prospects for the future

Polio eradication is feasible based on sustained interruption of WPV type 2 transmission since 1999, and on the success in interrupting transmission in all but four countries, including termination of

transmission in some of the most difficult areas of northern India where lower efficacy of OPV has been a major problem. However, major obstacles to success still must be overcome, including sustaining political commitment in all countries with ongoing WPV transmission or at risk of WPV importations, global support to assure mobilization of adequate resources to meet program needs, improving the quality of SIAs and routine immunization programs in countries, and overcoming vaccine failure in northern India.

The Global Polio Eradication Initiative, spearheaded by the WHO, Rotary International, the US CDC and The United Nations Children's Fund (UNICEF), has been aided by the Bill and Melinda Gates Foundation more recently, and the ongoing support of many development agencies, private enterprises and the endemic country governments. Lessons learned concerning what worked and what did not work in past efforts have been used to plan carefully in full concert with the government authorities in affected countries, to track indicators of progress more carefully than ever before, and to make changes in program implementation when appropriate. The polio eradication partnership has planned 3 years of intensive activities during 2010–2012 targeting foci of persistent WPV transmission in each country [102]. Implementation approaches include increased engagement and accountability of local leaders, predominant use of bOPV in SIAs, enhancing attention to migrant and other underserved populations, synchronizing SIAs across borders over large areas at risk, improving monitoring of SIA quality and enhancing efforts to strengthen routine

immunization. Research is underway to improve SIA implementation; examine causes of vaccine failure (e.g., enteric and parasitic infections) and potential measures to increase vaccine effectiveness (e.g., zinc-replacement therapy to reduce or prevent acute diarrheal disease); explore the potential role of IPV in accelerating polio eradication; evaluate the role of reinfection of older individuals in maintaining WPV transmission; and assess appropriate immunization and surveillance strategies in the post-eradication era. The immediate challenges include financial shortfalls that could seriously limit implementation of crucial SIAs, complacency where there have been signs of progress, inapparent transmission due to known or hidden surveillance weaknesses, continued nonengagement by some local authorities and continued inability to vaccinate children in areas of insecurity. If these are adequately faced, the funds and effort necessary to reach polio eradication are insignificant when compared with the long-term costs of accepting the status quo.

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