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COMMENTARY
Poliomyelitis: residual hurdles to global eradication

Paola Stefanelli[1,2], Gabriele Buttinelli[2] and Giovanni Rezza[2]

[1]WHO Polio Regional Laboratory for Europe, c/o Istituto Superiore di Sanità, Rome, Italy
[2]Dipartimento di Malattie Infettive, Parassitarie ed Immunomediate, Istituto Superiore di Sanità, Rome, Italy

Abstract
The global eradication of polio is close to achieving success. However, transmission of wild poliovirus persists in countries where the disease is endemic, and outbreaks may also occur in previously polio-free countries where population immunity is not maintained. To achieve polio eradication, several key actions are required: (1) to detect any poliovirus transmission, (2) to strengthen immunization systems and withdraw all oral polio vaccines from use, (3) to contain polioviruses and certify interruption of transmission, and (4) to sustain ongoing public health programs. In this context, residual hurdles to global polio eradication have been identified, from unstable political situation in affected countries to population movements from and to endemic areas, and opposition to immunization strategies. Global efforts are needed in order to promote routine immunization campaigns and large-scale vaccination rounds, which may provide direct protection of individuals and minimize virus circulation.

Key words
- poliovirus
- acute flaccid paralysis
- vaccination
- eradication

In 1988, the World Health Assembly adopted a resolution that committed all countries to polio eradication by the year 2000, launching the Global Polio Eradication Initiative (GPEI). Since then, several WHO Regions have been certified polio-free, including the Americas (in 1994), the Western Pacific Region (in 2000), the European Region (in 2002), and the South-East Asia Region, which includes the Indian subcontinent and Indonesia (in 2014). Importantly, the circulation of type 2 wild poliovirus (WPV) has been successfully stopped since 1999. Then, since November 2012, when the last WPV3 case was reported in Nigeria, WPV1 has been the only circulating wild type virus. Overall, more than 15 million cases of paralysis have been prevented and an estimated 1.5 million childhood death avoided through the administration of vitamin A during polio prevention activities [1].

Although a great success has been achieved, with a decrease in the incidence of paralytic polio from an estimated 1000 children per day in 1988 to about 400 in 2013, progress towards eradication has been slower than expected [2]. Up to now, polio remains endemic in Pakistan and Afghanistan, that reported 54 and 14 cases, respectively, in the year 2015. In 2016, only 14 cases have been reported in Pakistan and 9 in Afghanistan so far, but in Nigeria, where no cases had been detected in 2015, 3 cases of paralytic polio have been recently identified [3].

Further information on the circulation of polioviruses is provided by environmental surveillance. At the end of May 2013, WPV1 closely related to strains circulating in polio endemic areas of Pakistan and to those isolated from sewage samples in Egypt in 2012 was detected in a sewage-treatment plant in the South district of Israel [4, 5]. In 2014-2015, WPVs were isolated from environmental samples collected in Nigeria, Pakistan, and Afghanistan [6], and in 2016, 5 out of 27 environmental samples from the Belucistan province of Pakistan were found positive for poliovirus strains which probably originated in Afghanistan. To this regard, it is worthwhile to mention that in Belucistan, where an anti-polio campaign having the aim of vaccinating about 2.4 million < 5 years old children is starting at the end of September, militants have repeated attacked polio teams, and a suicide bombing outside a polio centre in Quetta's Satellite Town area killed 14 people, including 13 policemen earlier this year (www.dawn.com/news/1285841/environmental-samples-test-positive-for-poliovirus-in-quetta-pishin-districts).

Thus, poliovirus circulation is still ongoing in restricted geographical areas. In accordance with the Global Polio Eradication Initiative (GPEI), a country may be defined as (1) "endemic", when indigenous WPV circulation has never stopped, (2) "outbreak", if indigenous WPV circulation has stopped but it is affected by outbreak of imported WPV or circulating vaccine-derived poliovirus (VDPV), or (3) key at-risk (for outbreaks), if no longer

Address for correspondence: Paola Stefanelli, Dipartimento di Malattie Infettive, Parassitarie e Immunomediate, Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Rome, Italy. E-mail: paola.stefanelli@iss.it.

poliovirus-infected, but at high risk of outbreaks.

The determinants of polio persistence may be represented by gaps in routine and supplemental vaccine coverage, poor vaccine efficacy (*i.e.*, monovalent vaccines may be more effective than trivalent vaccines against specific types, especially in developing countries where interference with other enteroviruses and failure to establish infection in children with diarrhea may commonly occur), and highly favorable conditions for the transmission of fecal-oral pathogens (*i.e.*, high population density and poor sanitation, which may also lead to a high prevalence of diarrhea) [7].

POLIO PERSISTENCE AND OUTBREAKS: THE ROLE OF VIOLENCE, CIVIL UNREST, LOCAL PUBLIC HEALTH EMERGENCIES AND SOCIAL DISRUPTION

Among the causes favoring the failure of vaccination programs against polio, the religious opposition by fundamentalists is one of the main factor, as reported in Nigeria, Pakistan, and Afghanistan [8]. In tribal areas of Pakistan, local Taliban have issued *fatwas* denouncing vaccination as an Western plot to sterilize Muslim populations; wild polio virus from endemic districts in Afghanistan reemerged in previously polio-free areas in Pakistan, where several polio vaccination workers had been shot and killed [9].

In Somalia, which had been polio-free for 5 years, the virus was re-introduced in 2013, causing almost 200 cases of flaccid paralysis [10]. Similarly to the three endemic countries, Somalia was affected by violence and insecurity, and population hostility towards health-care workers, with coverage with 3 doses of OPV vaccine < 50% [11].

Social disruption due to civil war, with consequent decline of vaccine coverage, has been a driver of a resurgence of polio in Syria, where tens of cases of paralytic polio occurred between 2013 and 2014. A case of WPV1 was identified also in the outskirts of Baghdad, that had been polio-free for 14 years [12, 13]. This outbreak, which probably originated in Pakistan, occurred almost simultaneously with another outbreak in the Horn of Africa, tempered the optimism due to the success achieved in polio control in India, where no cases had been reported in the last 3 years.

Major epidemic events causing a collapse of health services may also affect vaccination coverage. A paradigmatic example is represented by the 2014-2015 Ebola outbreak occurred in three West-African countries (Guinea, Liberia, and Sierra Leone). To this regard, *promed*, on October 13, reported about 6 cases of suspected polio occurring in the Nimba province of Liberia (www.bushchicken.com/health-authorities-suspect-cases-of-polio-in-nimba/).

Although the estimations for vaccination coverage in Sierra Leone, Guinea and Liberia already painted a grim picture, the Ebola outbreak probably exacerbated the problem favoring the collapse of health services and the further drop of vaccination rates.

THERE IS A RISK FOR EUROPE?

To what extent imported polio cases pose a threat to the health of European citizens is matter of debate. The last endemic case of paralytic polio in the WHO European Region was reported in Turkey in November 1998, but a large outbreak of about 500 cases of poliomyelitis, due to a WPV1 imported from India, occurred in Tajikistan in 2010 [14]. In today European Union countries, an outbreak of 71 cases (59 paralysis and 2 death) occurred in an unvaccinated religious community in the Netherlands in 1992 [15], whereas other 3 cases were identified among Roma children in Bulgaria in 2001 [16]. These episodes remind us that reintroduction of polioviruses cannot be completely ruled out, and that maintaining high coverage of immunization is key to avoid the spread of the virus, especially among vulnerable population groups. To this regard, recent data from Italy report a vaccination coverage below 95%, which is considered the acceptable threshold for polio elimination (www.salute.gov.it/portale/documentazione/p6_2_8_3_1.jsp?%20lingua=%20italiano%20&id=20).

VACCINE-DERIVED PARALYTIC POLIOVIRUS CIRCULATION: THE PREVENTION PARADOX

Thanks to vaccine use, the burden of polio has been strongly reduced. However, the use of OPV is not free from rare but sometimes severe adverse events. First of all, OPV may revert to neurovirulence, leading to the development of cases of vaccine-associated paralytic poliomyelitis (VAPP) among vaccine recipients and their contacts (risk of VAPP: 1 per 900 000 first doses, with a 25-fold decline for further doses). Secondly, during prolonged infection in persons with primary immunodeficiency disorders or during outbreaks in settings with low OPV coverage, genetically divergent (> 1% divergence for PV1 and 3, and > 0.6% for type 2) VDPV may emerge. VDPVs may cause paralytic polio and have the potential for sustained circulation [17]. In particular, the risk of cVDPV strains emerging from OPV is higher when polio vaccination coverage is low.

Experience acquired with a large outbreak of type 2 cVDPV in Nigeria demonstrated that the pathogenicity and the severity of paralytic disease, as well as the transmissibility, are similar to those of WPVs [18]. Thus, interrupting the transmission of a cVDPV may require measures and level of protection similar to those needed to control an outbreak caused by WPV.

In the last decade, several sporadic cases and outbreaks due to circulating VDPV (cVDPV) were reported. At least five independent cVPDV2 outbreaks occurred in Pakistan since 2012, and several events peaking in 2009, followed by low-level circulation, were detected in Nigeria. Small clusters due to cVDPV2 and cVDPV1 were detected in South Sudan and in Madagascar, respectively [19].

In Europe, no cases of cVDPV were reported since the year 2000 until the end of August 2015, when two cases of paralytic poliomyelitis caused by cVDPV1 were detected in Ukraine [20].

ENVIRONMENTAL SURVEILLANCE: PROS AND CONS

Taking into account both the epidemiological opportunities and the potential risks of failure, the Polio

Eradication and Endgame Strategic Plan 2013-2018 was developed by WHO, with the aim eradicating both wild polioviruses and VDPV [21].

Enhanced environmental surveillance may be a useful early warning tool for the detection of polio virus circulation; however, it may be difficult to sustain financially in many countries [22], it does not provide convincing evidence of actual transmission in humans, and its methods are not yet standardized [23].

However, the identification of poliovirus, either WPV or cVDPV, is indicative of pockets of susceptibles (unvaccinated or incompletely vaccinated persons) in an area where individuals infected with the virus contribute to the transmission cycle amongst other susceptibles. As soon as the number of reported polio cases decreases, environmental surveillance (testing sewage for polioviruses) becomes key to supplement AFP surveillance in order to detect early events and unapparent WPV and/or VDPV circulation [6].

CONCLUSIONS

Despite significant progress in the global polio eradication efforts, polio outbreaks may occur until the transmission of the poliovirus will be stopped globally. In 2015, only 3 countries continue to have endemic circulation of wild polio virus: Afghanistan, Pakistan, and Nigeria. However, other regions in the world are still considered at risk for polio outbreaks [3]. All countries, in particular those characterized by population movement and contact with polio-affected countries, need to strengthen the surveillance of cases of acute flaccid paralysis (AFP), in order to rapidly detect any virus importation and to facilitate a rapid response. In this context, high routine immunization coverage is required to minimize the consequences of virus reintroduction and reactive vaccination strategies are needed in case of outbreaks. Early detection and effective response to the emergence of VDPV is also a key to the maintenance of the polio-free status. To this end, international organizations, goverments, and stakeholders need to join in a global effort to devise effective eradication strategies.

Conflict of interest statement

There are no potential conflict of interest or any financial or personal relationships with other people of organization that could inappropriately bias conduct and findings of this study.

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