Emerging Problems Impeding the Elimination of the Last Polioviruses: Silent Circulation of Wild Strains in a Well-Immunized Population

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(See the Major Article by Shulman et al on pages 1057–64.)

Keywords. poliomyelitis; vaccine; eradication; environmental surveillance.

Despite high polio vaccine coverage, Israel recently experienced a silent surge in the transmission of wild poliovirus in the population. In this issue of Clinical Infectious Diseases, Shulman and colleagues report interesting data about the antigenic and pathogenic features of the poliovirus strain circulating in that country.

Poliomyelitis, the causative agent of poliomyelitis, replicates mainly in the tonsils and in the small intestine. It is most often transmitted by the fecal–oral route and is extremely contagious. In most cases, replication of the virus in infected people remains asymptomatic or gives rise to only mild symptoms [1]. Paralytic poliomyelitis is relatively rare, affecting between 1 in 200 and 1 in 2000 infected people depending on the serotype of the virus (1, 2, and 3).

Two vaccines effectively prevent poliomyelitis. The inactivated injectable polio vaccine (IPV) was developed by Jonas Salk through the chemical inactivation of neurovirulent strains of the 3 serotypes; it is very safe and induces a strong and protective general antibody response. The live attenuated oral polio vaccine (OPV) was developed by Albert Sabin and induces a long-term protective response; this response includes an effective intestinal immunity that restricts interhuman circulation and replication of the virus. However, a problematic aspect of OPV is a consequence of the genetic instability of the 3 attenuated strains (Sabin 1–3). Multiplication of OPV strains in vaccinees allows their genetic drift and loss of attenuation. Consequently, neuroviral vaccine-derived polioviruses (VDPVs) can be excreted for years by chronically infected immunodeficient individuals (iVDPVs). In addition, pathogenic circulating vaccine-derived polioviruses (cVDPVs) can emerge following the interhuman circulation of OPV strains in underimmunized populations [2]. Nevertheless, as OPV can be distributed by nonmedical personnel, is cheap, and, above all, limits the interhuman circulation of the virus, it has been used as the main tool of the vaccination campaigns in developing countries, part of the global poliomyelitis eradication initiative launched by the World Health Organization (WHO) in 1988. Surveillance of the disease has been mainly based on virological investigations of stool samples from patients with acute flaccid paralysis (AFP). Few infected people develop the paralytic disease, so it is essential to detect, accurately and rapidly, all AFP cases so as to facilitate programs of vaccination with OPV as quickly as possible and thereby stop outbreaks by interrupting poliovirus circulation. This AFP surveillance is implemented by a global network of >150 laboratories, all using standardized methodologies and reagents.

Vaccination campaigns and surveillance have been largely effective: the incidence of poliomyelitis worldwide has decreased by >99% since 1988. The wild type 2 strains have been eradicated, and only 3 countries in the world (Nigeria, Pakistan, and Afghanistan) are still endemic for poliomyelitis due to local wild viruses. In addition, the recent eradication of poliovirus from India and the probable disappearance of wild type 3 viruses from the planet allow us to be reasonably optimistic about the eradication of the last wild type 1 polioviruses in the near future [3].

Nevertheless, over the last 15 years, the program has been facing serious issues: first, it has been difficult to improve polio vaccine coverage in the last endemic countries; and second, maintaining satisfactory
vaccine coverage in poor developing countries from which the wild endemic strains have already disappeared has proved problematic. Indeed, low vaccine coverage allows both the importation of polioviruses from endemic countries and the local emergence of cVDPVs.

Vaccine strategies have been modified to overcome these issues. Type 1 and type 3 monovalent OPVs and bivalent types 1 and 3 OPV have been used to increase type-specific seroconversion and to reduce the use of the Sabin 2 strain, which is the main source of cVDPVs. Most developed countries with the means to maintain and check vaccine coverage switched from OPV to IPV to prevent the occurrence of very rare cases of OPV-associated paralytic poliomyelitis and new iVDPVs.

Because the disease-to-infected individual ratio is low, it was considered necessary to improve the detection of polioviruses circulating in population, allowing action even before the occurrence of the first poliomyelitis cases. Thus, environmental surveillance, based on testing for polioviruses in sewage, has been set up in some countries to complement AFP surveillance [4]. Indeed, in endemic countries, there is a good correlation between the presence of wild poliovirus in AFP cases and that in sewage. This approach has also proved to be effective for detecting any widespread circulation of wild polioviruses in the absence of AFP cases. In addition, highly modified VDPVs, probably iVDPVs, have been found in sewage in developed countries only using IPV, including Finland, Estonia, and Israel. In Israel, similar recombinant VDPV lineages were found recurrently for 15 years, in the same sewage system used by >1 million people, underlining the striking sensitivity and accuracy of the method [5].

Israel has been poliomyelitis-free since 1989 and, since 2005, only IPV has been used (vaccine coverage >95%). In addition to AFP surveillance, there has been country-wide, monthly sewage surveillance. In February–March 2013, a wild type 1 poliovirus (WPV1) lineage was discovered in sewage samples collected in 2 cities in southern Israel (Rahat and Beer Sheva) [6]. The viral strains were closely related to a WPV1 circulating in Pakistan (WPV1-South Asian [SOAS]) in 2012 and isolated in Egypt the same year [7]. Until July 2013, WPV1-SOAS was detected persistently in 10 of the 47 environmental surveillance sites (southern and central Israel) and intermittently in a further 8; it was also found in stool samples from healthy individuals, indicating sustained transmission. IPV does not induce a significant mucosal immune response, and so public health policymakers decided to use bivalent types 1 and 3 OPV. One bivalent OPV dose was given to each member of the entire population in August 2013 and a second dose was given in October in the most affected areas. This was followed by the gradual disappearance of WPV1-SOAS, and the strain has not been detected in Israel since April 2014 (Poliomavirus Weekly Update, 24 December 2014, WHO).

To elucidate the reasons for the substantial silent circulation of WPV1-SOAS in the well-immunized Israeli population, Shulman et al investigated the antigenic profile of isolates and their neurovirulence in transgenic mice expressing the poliovirus receptor (Tg-PVR mice). They determined sequences and conducted neutralization experiments using murine Sabin 1–specific monoclonal antibodies (mAbs): they thereby found that 3 of the 4 antigenic sites differed from those in the attenuated Sabin 1 strain or its Mahoney neurovirulent parental strain used to make IPV. Only mAbs specific for antigenic site 4 neutralized WPV1-SOAS. Despite these antigenic differences, most sera from rodents immunized with a single dose of IPV also showed lower neutralization titers against WPV1-SOAS than against Sabin 1 and Mahoney strains. The authors concluded that antigenic differences between virus strains used in vaccines and WPV1-SOAS may have facilitated the spread of the wild virus in the immunized population. However, a single dose of IPV was sufficient to protect Tg-PVR mice against a lethal dose of WPV1-SOAS. Moreover, it is likely that the immune response following vaccination with bivalent OPV was the determinant factor that contributed to stopping WPV1-SOAS transmission in Israel. Antigenic characteristics similar to those of WPV1-SOAS strain, with modifications in antigenic sites 1–3, have been described for a wild poliovirus type 1 strain that was involved in a polio outbreak in Congo in 2010 [8]. The abnormally high mortality rate that was reported, mostly involving young adults, was believed to be linked to immunization gaps in a particular age group and reduced protection conferred by OPV against this epidemic strain. Nevertheless, the epidemic stopped following OPV campaigns [9].

The pathogenicity of the Israeli WPV1-SOAS was evaluated in Tg-PVR mice: the virus was found to be slightly less neurovirulent than other wild or VDPV strains tested. WPV1-SOAS is closely related to the wild type 1 poliovirus that caused a poliomyelitis outbreak in an undervaccinated population in Syria in 2013. It is therefore probable that the absence of polio cases in Israel was a consequence of high vaccine coverage rather than the decreased neurovirulence of the epidemic strain.

Thus, the substantial transmission of WPV1-SOAS in a population well-immunized with IPV stopped following OPV campaigns. This success underlines the differences in the qualities of the 2 available polio vaccines: IPV protects against the disease, and OPV mimics the replication of wild strains and induces a local intestinal immune response,
efficiently limiting viral transmission [10]. Ideally, a new IPV inducing a broader antigenicity and a potent local immune response, or a genetically stabilized OPV, should be developed. In the absence of a new vaccine, it is likely that both existing vaccines will be needed for a long period of time, including into the posteradication era: IPV to protect humans against the possible reemergence of the disease, without promoting VDPVs, and OPV to block poliovirus circulation and extinguish possible outbreaks.

Above all, this silent poliovirus circulation in Israel illustrates how countries using IPV are at risk of importation and subsequent intense transmission of polioviruses (wild or VDPVs). Consequently, all regions continue to need competent scientists capable of implementing rigorous surveillance and organizing rapid and efficient responses in emergency situations. Finally, this story demonstrates the effectiveness of environmental surveillance for detecting the silent circulation of dangerous enteric pathogens in the population before the first case of disease. Regular surveillance, in particular in large cities and communities known to be at risk of poliovirus importation, should be set up and pursued.

Note

Potential conflict of interest. Both authors: No reported conflicts. Both authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References