SHORT REPORT
Failure to detect infection by oral polio vaccine virus following natural exposure among inactivated polio vaccine recipients

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(Accepted 13 January 2007; first published online 22 March 2007)

SUMMARY
While oral polio vaccine (OPV) has been shown to be safe and effective, it has been observed that it can circulate within a susceptible population and revert to a virulent form. Inactivated polio vaccine (IPV) confers protection from paralytic disease, but provides limited protection against infection. It is possible, then, that an IPV-immunized population, when exposed to OPV, could sustain undetected circulation of vaccine-derived poliovirus. This study examines the possibility of polio vaccine virus circulating within the United States (highly IPV-immunized) population that borders Mexico (OPV-immunized). A total of 653 stool and 20 sewage samples collected on the US side of the border were tested for the presence of poliovirus. All samples were found to be negative. These results suggest that the risk of circulating vaccine-derived poliovirus is low in fully immunized IPV-using populations in developed countries that border OPV-using populations.

In 1988 the World Health Assembly passed a resolution committing to the global eradication of polio. At the time of this resolution, around 350,000 cases occurred annually in 126 countries. Today, polio is endemic in only four countries and newly reintroduced in 21 more, with 1831 cases occurring in 2005. As we near the goal of eradication, attention is increasingly directed toward post-eradication issues. One such issue is how to discontinue the use of oral polio vaccine (OPV).

OPV has proven to be safe and effective and has been the main tool in the eradication effort. One of its advantages is the ability to be transmitted from recipients, thus providing a boost in immunity to contacts of vaccine recipients. In a very small percentage of cases, however, OPV can result in vaccine-associated paralytic poliomyelitis (VAPP). As a country eliminates wild poliovirus and continues to use OPV, VAPP makes up a higher proportion of paralytic polio cases. Because of this risk of VAPP, many developed countries that have eliminated polio transmission have switched to using inactivated polio vaccine (IPV), which does not cause VAPP. The United States introduced a sequential immunization schedule of both OPV and IPV in 1997, and switched to the exclusive use of IPV in 2000.

It is well known that OPV reverts to a more virulent form with replication. To date, circulating vaccine-derived poliovirus (cVDPV) has been responsible for seven outbreaks of poliomyelitis. In addition, instances of single cases or poliovirus-positive sewage
samples have been found in which the poliovirus has $\geq 1\%$ genetic divergence from the parent Sabin virus strain in the VPI region of the viral genome (the definition of VDPV) [1, 2], consistent with about 1 year or more of viral replication. In all cases, the outbreaks occurred in populations in which a large number of susceptible persons had built up because of gaps in immunization.

IPV provides good protection against disease, but does not confer complete protection against infection. Early studies showed that both wild-type and vaccine poliovirus are easily transmitted from an infected person to IPV-immunized persons in a household setting [3]. IPV was also found to offer minimal protection against infection following a challenge dose with OPV [4]. Under conditions of community exposure, where contact with an infected person is not as close, IPV was shown to confer some protection against poliovirus infection [3, 5].

Because of suboptimal antibody response to IPV, by the late 1980s the original IPV was replaced by an enhanced formulation with increased potency. At the time the enhanced IPV was introduced, it was only in use in some western European countries that had already eliminated wild poliovirus. Studies were done in which recipients were given a challenge dose of monovalent OPV to test enhanced IPV’s ability to protect against infection [6]. These studies showed that the enhanced IPV conferred less protection against infection than OPV, but it is difficult to determine how the virus titre of the challenge dose compares with the amount of virus that would be encountered in a natural exposure.

Because IPV confers limited protection against infection, the possibility exists for wild or vaccine poliovirus to circulate undetected in persons with IPV-induced immunity. If vaccine virus circulates among an IPV-immunized population, the potential would exist for it to accumulate mutations and become a virulent cVDPV. The risk for vaccine virus circulation and the development of virulent VDPVs should be greatest in situations in which an IPV-immunized population has extensive contact with an OPV-immunized population, raising the possibility that IPV-immunized children could become infected with vaccine virus from children who had recently received OPV. In this study we determine whether vaccine virus (OPV or VDPV) is circulating among fully IPV-immunized persons (three or more IPV doses) in the United States where it borders the OPV-immunized population of Mexico.

Enrolment took place in Cameron and Hidalgo counties of Texas, which lie along the border with Mexico in the southernmost part of the state. Communities in this area are 85–90% Hispanic. Many have family contacts in Mexico and cross-border travel is extensive. IPV coverage in these counties is over 90%. OPV coverage in the Mexican state of Tamaulipas, which borders the study counties, is also over 90%.

Because the purpose of this study was to assess transmission to or among children who had acquired immunity through IPV vaccination, we restricted enrolment to those who had received at least three IPV doses to maximize the number of children with IPV-induced neutralizing antibodies against poliovirus. Vaccine history was by oral report from a parent or guardian. Children who were born after 1 January 2000, lived in one of the two study counties, had received at least three doses of IPV, and had never received OPV were enrolled in the study from 12 public and private clinics in Hidalgo and Cameron counties of Texas. These clinics were chosen because of accessibility of the patient population. Most are Women with Infant Children clinics, a public assistance programme, and serve a lower socioeconomic level population. The parent or guardian of the child was approached in the clinic by a study interviewer who explained the study in English or Spanish, determined eligibility, and obtained consent. Children were selected for enrolment by a convenience sample. This study was approved by the institutional review boards of the Centers for Disease Control and Prevention and the Texas Department of State Health Services (TDSHS).

The parent or guardian of each enrolled child was given instructions on collecting a stool specimen and given a collection kit. The samples were to be kept refrigerated until returned to the interviewer. The interviewer transported the samples in a cooler to the TDSHS regional office where they were stored at $-70^\circ$C until being shipped on dry ice to the TDSHS laboratory for testing.

Twenty sewage samples were collected from 17 sites in the study area during the third week of September, 1 year prior to the collection of the stool samples. These sites were selected to provide adequate coverage of the main population areas covered in the two study counties. Included in the sites were the sewage systems covering the clinics from which the study participants were recruited. Each sample was collected at the main inlet to the community sewage...
treatment plant. The 1-litre samples were stored at −20 °C before being transported on dry ice to the University of North Carolina School of Public Health for testing.

Stool samples were processed using the following procedure. A stool aliquot was added to 6 ml of Hank’s Balanced Salt Solution (BSS). The specimen was vortexed, centrifuged for 20 minutes at 1500 g in a refrigerated centrifuge, and then the supernatant transferred to a glass tube. A garamycin/amphotericin B solution was added to the specimen giving a final concentration of 100 µg of garamycin and 10 µg of amphotericin B per millilitre of specimen. The sample was incubated at 4 °C for 1 h and then inoculated onto cell cultures. Isolation procedures were then followed according to the WHO Polio Laboratory Manual [7]. Sewage samples were processed and tested using procedures described elsewhere [8].

A total of 664 children were enrolled. Five specimens were inadvertently discarded and specimens were not collected from four children. Two additional children had reported ages inconsistent with the number of reported IPV doses (2 and 4 months) leaving 653 children for analysis. The median age of the children whose data were analysed was 26 months, ranging from 6 months to 46 months; 346 (53%) were male. In total, 617 (95%) reported being Hispanic, three (0.5%) non-Hispanic, two (0.3%) both, and two (0.3%) other. Twenty-eight (4%) did not report an ethnicity.

All sewage samples tested negative for the presence of poliovirus while 18 of the 20 (90%) samples tested positive for non-polio enterovirus. All 653 stool samples were negative for poliovirus, giving an upper 95% confidence bound for the viral shedding rate of 0.5%. Sixty (9%) children tested positive for non-polio enterovirus.

The results of the stool and sewage sample tests indicate that OPV or VDPV transmission among fully IPV-immunized children. It is possible that transmission may be taking place at low levels in younger children with fewer IPV doses or other under-immunized groups, although this appears unlikely. Moreover, because OPV coverage is high in Mexico (98% for three doses of OPV in children aged <1 year in 2004), viral shedding may be reduced over what would be found in children with fewer OPV doses, reducing exposure for the IPV-immunized children.

The results of this study suggest that a developed country that uses IPV and borders an OPV-using country may not be at risk for becoming a reservoir for cVDPV. It is possible that OPV can still be transmitted within pockets of unvaccinated persons within a vaccinated population. This was illustrated most recently by the identification of circulating VDPV in an Amish community in Minnesota [10]. Further work is needed to determine whether IPV-immunized populations in developing countries can sustain OPV or VDPV circulation.

DECLARATION OF INTEREST
None.

REFERENCES


