SHORT REPORT

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

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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 \( > 1\% \) genetic divergence from the parent Sabin virus strain in the VP1 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 systems.
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 
centration 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 re-
ported 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 is not in widespread 
circulation in the fully IPV-immunized population 
despite extensive contact between the Mexican and 
US populations. The sensitivity of the stool testing to 
detect poliovirus is indicated by the ability to detect 
non-polio enteroviruses, although the percentage 
positive was just under the WHO’s target of 10% for 
acute flaccid paralysis surveillance for polio. This 
lower rate of non-polio enterovirus infection is not 
usual for a temperate climate. Similarly, non-polio 
enterovirus was detected in a high percentage of the 
sewage samples, indicating the sensitivity to detect 
circulating poliovirus. All samples were collected 
during September–October, which is during the peak 
of the enterovirus transmission period. It is possible 
that some transmission takes place from OPV re-
cipients to IPV recipients or between IPV recipients, 
but at a level too low to maintain circulation or to 
detect. This finding is consistent with experience in 
other IPV-using countries [9].

It is possible that populations in developing 
countries with conditions more favourable for polio-
virus circulation may be able to sustain vaccine virus 
circulation after switching to IPV. The role of IPV 
post-eradication in these countries is unknown at 
this time. The main obstacles to using IPV in these 
settings, particularly in mass campaigns, are cost and 
logistic difficulties. These may change if new dosing 
regimens and administration technology such as the 
use of fractional doses of IPV and needleless injection 
systems prove to be feasible and effective.

This study was designed to investigate 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 trans-
mittted 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.

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