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Poliomyelitis outbreaks in Angola genetically linked to India: Risk factors and implications for prevention of outbreaks due to wild poliovirus importations

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ABSTRACT

We conducted an investigation of two outbreaks of poliomyelitis in Angola during 2007–2008 due to wild poliovirus (WPV) genetically linked to India. A case-control study including 27 case-patients and 76 age- and neighborhood-matched control-subjects was conducted to assess risk factors associated with paralytic poliomyelitis, and epidemiologic links to India were explored through in-depth case-patient interviews. In multivariable analysis, case-patients were more likely than control-subjects to be undervaccinated with fewer than four routine doses of oral poliovirus vaccine (adjusted matched odds ratio [aMOR], 4.1; 95% confidence interval [CI], 1.2–13.6) and have an adult household member who traveled outside the province of residence in the 2 months preceding onset of paralysis (aMOR, 3.2; 95% CI, 1.2–8.6). No epidemiologic link with India was identified. These findings underscore the importance of routine immunization to prevent outbreaks following WPV importations and suggest a possible role of adults in sustaining WPV transmission.

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1. Introduction

When the World Health Assembly established the Global Polio Eradication Initiative in 1988, approximately 350,000 cases of paralytic poliomyelitis per year occurred in >125 endemic countries. By 2008, the number of poliomyelitis cases had declined to 1659 cases, and only four countries (Afghanistan, India, Nigeria, and Pakistan) had never interrupted indigenous wild poliovirus (WPV) transmission. However, progress towards poliomyelitis eradication has been complicated by the reintroduction of WPV from endemic countries to countries that were previously polio-free. During 2008–2009, 21 countries in Africa that had previously interrupted indigenous WPV transmission reported cases of poliomyelitis due to WPV originating from Nigeria or India [1,2].

Angola, located in south central Africa, detected its last indigenous WPV case in 2001 and was polio-free from 2002 to 2004. Key to the successful interruption of indigenous WPV transmission were the country's immunization strategies, including routine vaccination and supplemental immunization activities (SIAs) with oral polio vaccine (OPV). Established in 1979, Angola's routine immunization schedule includes four doses of trivalent OPV (tOPV) administered at birth, and at 2, 4, and 6 months of age. In addition, nationwide SIAs targeting all children <5 years of age for additional doses of OPV have been held at least twice per year since 1996. Despite these immunization activities, during 2005–2008 Angola received three genetically distinct WPV importations from India, which resulted in outbreaks of paralytic poliomyelitis, reestablished WPV transmission (transmission for >12 months after importation), and the subsequent reintroduction of WPV to other countries in central Africa [2,3].

To understand why Angola has been the site of entry for multiple WPV importations from India and why WPV transmission within Angola persisted, we conducted a field investigation in October–November 2008.

2. Methods

We reviewed routine immunization data from January 2005 to June 2008 and SIA data from January 2005 to November 2008 provided by the Expanded Program on Immunization (EPI) offices at Angola Ministry of Health and World Health Organization (WHO) Angola. Administrative vaccination coverage with OPV for routine immunization and SIAs were calculated by dividing the reported

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number of doses administered by health care providers by the estimated number of eligible children in the population. Official population estimates were provided by the Angola Ministry of Health.

Possible cases of paralytic poliomyelitis are detected through Angola's national acute flaccid paralysis (AFP) surveillance system, which was established in 1997. An AFP case is defined as the sudden onset of weakness and floppiness in any part of the body in a child <15 years of age or suspected poliomyelitis in a person of any age. Upon identification of a case, a surveillance officer conducts an investigation, including collection of stool samples for virologic testing for the presence of poliovirus and a follow-up examination approximately 60 days after onset to assess for residual paralysis. Poliovirus isolation, intratypic differentiation, and genetic analysis are performed using standard protocols at the WHO Regional Reference Laboratory for Poliomyelitis in Johannesburg, South Africa [4,5].

A matched case-control study to evaluate risk factors associated with poliomyelitis in Angola was conducted in October–November 2008. A case was defined as a laboratory-confirmed wild poliovirus infection genetically linked to the 2007 or 2008 importations in a patient identified in the national AFP surveillance database who had onset of AFP from April 2007 to September 2008. Case-patients were traced using contact information obtained from AFP surveillance case investigation forms, and from district surveillance officers and health workers. There was only one case-patient per household. Three age- and neighborhood-matched control-subjects were selected for each case from non-case households surrounding the case household using a random direction and random number list, and were matched within 6 months of the case-patient's age. No more than one control-subject was selected from each household.

Verbal consent was obtained and a standard questionnaire was administered to subjects ≥15 years of age or to caregivers of subjects <15 years of age. The standard questionnaire included questions about demographic information, number of OPV doses received, and travel and other exposures, including exposure to travelers, markets, airports, and train stations, within 2 months prior to AFP onset. In addition, a supplemental household questionnaire, which asked more detailed questions about travel and international exposures, was administered for case-patients. Information gathered from the supplemental questionnaire and epidemiologic links to India among case-patients enrolled in the case-control study were explored in a descriptive analysis.

Routine vaccination history was obtained from the caregiver-held vaccination card or by caregiver recall when the card was not available. History of SIA doses was obtained by recall only. Because SIAs may use tOPV, monovalent OPV type 1 (mOPV1), or monovalent OPV type 3 (mOPV3), it was necessary to calculate the number of type-relevant SIA doses received. The number of type-relevant SIA doses received (mOPV1 or tOPV doses for WPV type 1 [WPV1] case-patients; mOPV3 or tOPV doses for WPV type 3 [WPV3] case-patients) was considered to be the number of SIA doses reported by the subject, but could not exceed the number of type-relevant SIA doses offered in Angola after the subject's birth, before the subject was 5 years of age, and before onset of AFP.

For the analysis, so that case- and control-subjects had comparable opportunity to receive all four routine OPV doses, control-subjects <6 months of age matched to case-patients ≥6 months of age at the time of AFP onset were excluded. Subjects with unknown routine vaccination history were classified as having fewer than four routine OPV doses. When total number of type-relevant OPV doses was calculated, subjects with unknown vaccination histories for birth dose, routine doses, or SIA doses were included, but the unknown histories contributed zero doses to the total number of doses.

Table 1
Estimated routine immunization coverage with the birth dose and three routine doses of trivalent oral polio vaccine (tOPV) among children by birth year, Angola, January 2005–June 2008.

Year	Birth dose of tOPV[a]	Three routine tOPV doses[b]
2005	58%	46%
2006	59%	44%
2007	76%	83%
January–June 2008	69%	75%[c]

[a] *Source*: Ministry of Health, Luanda, Angola, October 2008.
[b] *Source*: WHO/UNICEF estimate for coverage with three routine tOPV doses given at 2, 4, and 6 months of age [12].
[c] WHO/UNICEF estimate for January–December 2008 [12].

Risk factors for poliomyelitis were evaluated in matched analysis using conditional logistic regression. Two separate multivariable models were created: one model used routine OPV doses as the vaccination variable and one model used total type-relevant OPV doses as the vaccination variable. Risk factors with Wald chi-squared p-value <0.10 in the univariate analysis were tested in the multivariable model, and the final multivariable models were created using backward elimination of variables with a p-value >0.05 in the model and whose elimination resulted in <10% change in the point estimate of the odds ratios for the variables remaining in the model. Forward selection models using the same criteria were created for the purposes of comparison. Vaccine effectiveness (VE) was estimated using the formula $VE = (1 - aMOR) \times 100$, where aMOR is the adjusted matched odds ratio for ≥4 OPV doses vs. <4 OPV doses. Because of the low case-to-infection ratio for poliovirus, the rare disease assumption is satisfied, the odds ratio is good estimate of relative risk, and this formula provides an acceptable estimate of vaccine effectiveness.

3. Results

3.1. Vaccination coverage

Reported administrative coverage with the birth dose of tOPV increased from 58% in 2005 to 69% in January–June 2008 and estimated coverage with three routine tOPV doses increased from 46% in 2005 to 75% in 2008 (Table 1). In addition, 14 national and 5 sub-national SIAs were conducted in Angola during 2005–2008, with reported administrative coverage ranging from 75% to 107% (Table 2, Fig. 1).

3.2. Confirmed poliomyelitis cases

During 2005–2008, a total of 49 laboratory-confirmed cases of poliomyelitis were reported in Angola, all of which had WPV isolates genetically related to one of the three WPV strains imported from India (Fig. 1). Following the first importation, a total of 13 WPV1 cases were reported during 2005–2007; the second importation resulted in 12 WPV1 cases reported during 2007–2008; the third importation resulted in 24 WPV3 cases reported during 2008.

3.3. Characteristics of study subjects

For the case-control study, 33 eligible cases were identified in the AFP database with AFP onset April 2007–September 2008. Of these, 27 (82%) case-patients were able to be traced and were enrolled in the study, along with 76 age- and neighborhood-matched control-subjects (81 control-subjects were interviewed, but 5 were excluded because they were <6 months of age and were matched with case-patients who were ≥6 months of age).