Vaccine-associated paralytic poliomyelitis in India during 1999: decreased risk despite massive use of oral polio vaccine

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Objective Vaccine-associated paralytic poliomyelitis (VAPP) is a rare but serious consequence of the administration of oral polio vaccine (OPV). Intensified OPV administration has reduced wild poliovirus transmission in India but VAPP is becoming a matter of concern.

Methods We analysed acute flaccid paralysis (AFP) surveillance data in order to estimate the VAPP risk in this country. VAPP was defined as occurring in AFP cases with onset of paralysis in 1999, residual weakness 60 days after onset, and isolation of vaccine-related poliovirus. Recipient VAPP cases were a subset with onset of paralysis between 4 and 40 days after receipt of OPV.

Findings A total of 181 AFP cases met the case definition. The following estimates of VAPP risk were made: overall risk, 1 case per 4.1 to 4.6 million OPV doses administered; recipient risk,1 case per 12.2 million; first-dose recipient risk, 1case per 2.8 million; and subsequent-dose recipient risk, 1 case per 13.9 million.

Conclusion On the basis of data from a highly sensitive surveillance system the estimated VAPP risk in India is evidently lower than that in other countries, notwithstanding the administration of multiple OPV doses to children in mass immunization campaigns.

Keywords Poliovirus vaccine, Oral/adverse effects/administration and dosage; Poliomyelitis/chemically induced/epidemiology; Paralysis/epidemiology; Poliovirus/isolation and purification; Risk assessment; India (*source: MeSH, NLM*).

Mots clés Vaccin antipoliomyélitique Sabin/effets indésirables/administration et posologie; Poliomyélite antérieure aiguë/induit chimiquement/épidémiologie; Paralysie/épidémiologie; Poliovirus/isolement et purification; Evaluation risque; Inde (*source: MeSH, INSERM*).

Palabras clave Vacuna antipolio oral/efectos adversos/administración y dosificación; Poliomielitis/inducido químicamente/epidemiología; Parálisis/epidemiología; Poliovirus/aislamiento y purificación; Medición de riesgo; India (*fuente: DeCS, BIREME*).

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Introduction

In 1988 the World Health Assembly resolved to eradicate poliomyelitis globally by 2000 (*1*). India began implementing polio eradication strategies in 1995 (*2*), and in 1999 introduced additional rounds of national immunization days (NIDs) and increased reliance on house-to-house visits for the administration of oral polio vaccine (OPV). The objective of NIDs is to decrease widespread poliovirus circulation rapidly by mass immunization campaigns with OPV, lasting only a few days and targeting all children under 5 years of age regardless of their vaccination history.

Vaccine-associated paralytic poliomyelitis (VAPP) is a rare adverse event following the administration of OPV. In England and Wales, the estimated risk of VAPP in 1985–91 was 1 case per 1.4 million OPV doses administered (*3*). In the USA, VAPP risk estimates ranged from 1 case per 2.5 million doses of OPV distributed in 1980–89 (*4*) to 1 case per 3.2 million doses distributed in 1973–84 (*5*). Data from the acute flaccid paralysis (AFP) surveillance system in Latin America showed an estimated VAPP risk of 1 case per 1.5–2.2 million doses administered in 1989–91 (*6*). These studies demonstrated that the risk was substantially increased following receipt of the first dose of OPV and that children with B-cell immunodeficiency disorders were at highest risk for VAPP (*4*). Reports from Romania (*7*, *8*) suggested that multiple injections could increase the risk of VAPP (provocation or aggravation poliomyelitis) and raised the question of whether mass immunization campaigns might be associated with an elevated VAPP risk.

In 1999 India accounted for over half the cases of polio occurring globally. The number of polio cases attributable to wild poliovirus infection in this country has rapidly declined as efforts to eradicate the disease have progressed. The proportion of cases of paralysis caused by receipt of OPV or contact with an OPV recipient can be expected to increase as the vaccine continues to be used extensively in both routine and supplemental immunization activities.

Except in Latin America in 1989–91 (*6*), VAPP risk has not been assessed in tropical countries where polio is endemic. A decrease in the immunogenicity of OPV has been reported in

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tropical climates (*9*). This could alter the risk of VAPP in developing tropical countries relative to estimates from the USA or Europe. In the present analysis, national AFP surveillance data are used to describe VAPP cases in India in 1999 and to estimate overall and recipient VAPP risk.

Methods

Study population

Active surveillance for AFP was established in October 1997. International performance standards were met and in May 1998 they began to be surpassed, i.e. the non-polio AFP rate was at least 1 case per 100 000 population under 15 years of age. AFP is defined as any case of acute-onset flaccid paralysis in a child under 15 years of age without another obvious cause, such as trauma, or any case of paralytic illness occurring in any person, regardless of age, in whom poliomyelitis is suspected. AFP cases are detected by active surveillance. This involves over 11 000 health care institutions reporting weekly (*10*).

When an AFP case is identified and reported to the surveillance system, epidemiological and clinical information is collected at both an initial investigation and 60 days after the onset of paralysis. Two stool specimens are collected within 14 days after the onset of paralysis for virological testing. All AFP cases reported to the surveillance system in 1999 were eligible for this analysis.

Case definition

AFP cases in which wild poliovirus was isolated from any stool sample were classified as confirmed polio cases and were excluded from the VAPP case definition. VAPP was defined as occurring in AFP cases if there was residual weakness 60 days after the onset of paralysis, if vaccine-related poliovirus was isolated from any stool sample, and if no wild poliovirus was isolated from any stool sample. A subset of recipient VAPP cases was defined as those VAPP cases with an interval of 4 to 40 days between the receipt of OPV and the onset of paralysis. There is no standard case definition of VAPP. An interval of 4–40 days was chosen to define recipient VAPP in order to improve comparability with previous studies (*6*). Because the available data from the Indian surveillance system did not include contact and exposure histories, VAPP cases not meeting the criteria for recipient VAPP were classified as non-recipient VAPP cases. Many of these would have been considered as cases of contact VAPP in other studies.

Data

The database of the Indian AFP surveillance system included demographic, virological and clinical information. The data were used to arrive at the final classification of confirmed or discarded cases of poliomyelitis.

All cases of AFP should be investigated within 48 hours of being reported. An investigator confirmed whether each case was one of AFP and completed a standard case investigation form. The data collected as part of the investigation included the date of onset of paralysis, the age of the child, its immunization history, and the clinical history and findings (signs and symptoms). Investigators also arranged for the collection of stool specimens and their transportation to the national polio laboratory network for virus isolation and subsequent differentiation of wild virus and vaccine-related strains (*11*). All the laboratories in the network underwent an annual accreditation process coordinated by WHO (*12*).

Standard procedures were used to isolate viruses from stool suspensions by culture in a rhabdomyosarcoma and HEp-2C cell monolayer (*13*). In the second half of 1999, Hep-2C cells were replaced by L20B cells (*14*). Neutralization tests involving the use of high-titre equine sera were performed in order to determine serotypes. Poliovirus isolates were further characterized as vaccine-related or wild by hybridization with genotypic probes (*15*) and by polymerase chain reaction analyses (*16*).

Risk estimates

Data from the national surveillance system showed that the non-polio AFP rate in children under 15 years of age was 1.8/100 000, well above the benchmark of at least 1 case per 100 000 required to demonstrate that an AFP surveillance system is operating with sufficient sensitivity to meet international standards. The risks of overall VAPP and recipient VAPP were estimated. The risk of recipient VAPP was further categorized as following first or subsequent OPV doses. In order to calculate the overall VAPP risk the estimated number of OPV doses administered via both routine immunization and NIDs was used as the denominator. Routine immunization in India includes three OPV doses given at 6, 10 and 14 weeks of age and a birth or zero dose for institutional births. On the basis of data for 1997–98 obtained from the Ministry of Health and Family Welfare it was assumed that, of the annual birth cohort of 25 million infants, 8.3 million (33.3%) were institutional births and that, of these, 6.1 million (73%) received four doses of OPV by way of routine immunization, giving a total of 24.3 million doses. For the remaining 16.7 million (66.7%) of the birth cohort, 73% (12.2 million) were assumed to have received three routine OPV doses, giving a total of 36.5 million routine doses. The total number of routine OPV doses administered in 1999 was thus estimated to be 60.8 million.

NIDs were held in January, October, November and December 1999. An additional subnational round was held in March 1999 in areas with confirmed wild poliovirus cases. The numbers of children under 5 years of age who received OPV in each of these rounds are given in Table 1. Approximately 672.6 million supplemental OPV doses were administered during NIDs in 1999. Altogether, therefore, some 733.4 million OPV doses were administered during the year, either routinely or during NIDs.

Table 1. **National and subnational immunization days, India, 1999**

Date	Children aged 0–5 years receiving OPV[a]
17 January 1999	134 889 848
14 March 1999[b]	106 937 384
24 October 1999	141 490 011
21 November 1999	142 263 569
19 December 1999	147 030 690
Total	**672 611 502**

[a] Oral polio vaccine.
[b] Subnational immunization day.

In order to calculate the risk of recipient VAPP following the first OPV dose it was assumed that all infants received at least one dose of OPV during the first year of life. Thus the birth cohort of 25 million in 1999 was used as the denominator. For the calculation of the VAPP risk following subsequent OPV doses the denominator was the number of OPV doses administered in 1999 minus the number of first doses, i.e. 708.4 million subsequent doses (733.4 million minus 25 million).

The data were analysed by means of Epi Info (v. 6.04, Centers for Disease Control and Prevention, Atlanta, Georgia, USA) and SAS (v. 6.12, Cary, North Carolina, USA). They are presented as means and standard deviations or as medians with ranges; t-tests for differences in proportions involved using the Yates corrected *P*-value or the two-tailed Fisher's exact *P*-value; the Kruskal–Wallis test was used for nonparametric comparisons. Statistical significance was defined as $P < 0.05$.

Results

A total of 9576 AFP cases were reported to the national surveillance system in India, in 1999. Of these, 4127 (43.1%) had residual weakness at follow-up examination 60 days after the onset of paralysis. The 952 cases in which wild poliovirus was isolated in at least one stool sample were excluded. The subsequent analysis was restricted to the 271 cases with vaccine-related poliovirus isolated in any stool sample. Of these, 87 cases (32.1%) in which OPV was received after the onset of paralysis and before stool collection and 3 cases (1.1%) with an unknown number of OPV doses were excluded. Thus there remained 181 VAPP cases which formed the basis for this analysis.

Of these cases, 60 (33.1%) developed paralysis between 4 and 40 days after receiving OPV and were classified as recipient VAPP. For 8 cases (4.4%) there was no information on the date of the last OPV dose and the number of OPV doses received; for 13 cases (7.2%) there was no information on the date of the last OPV dose but it was known that OPV had been administered at least once. Two risk calculations were made, one including the 21 cases with unclear immunization histories and one excluding them, so as to obtain a range of overall VAPP risk.

Total VAPP cases

For the 181 total VAPP cases the median age was 2 years (range 37 days to 13.4 years), the median number of OPV doses before the onset of paralysis was 4 (range 0–14), and 87.3% of the cases occurred in children under the age of 5 years (Table 2). Fever was present at the time of onset of paralysis in 67.4% of the VAPP cases; 70.2% of the cases had asymmetric paralysis. Where only a single virus was isolated, vaccine-related poliovirus type 3 (33.1%) and type 1 (32.6%) were most frequently isolated in the stools of VAPP cases, followed by poliovirus type 2 (21.5%) (Table 3). Mixtures of two or three poliovirus types were present in 12.7% of all VAPP cases. Of the 23 cases in which mixtures were isolated, nine (39.0%) had mixtures of types 1 and 3, six (26.1%) had mixtures of types 1 and 2, six (26.1%) had mixtures of types 2 and 3, and two (8.7%) had mixtures of types 1, 2 and 3. The age distribution of cases is given in Fig. 1.

Recipient VAPP cases

The median age of the 60 recipient VAPP cases was 1.2 years (range 39 days – 2555 days (7 years)) and the median number of OPV doses was 4 (range 1–14) (Table 2). Asymmetric paralysis was present in 68.3%; 65.5% had fever at the time of onset of paralysis; 93.3% were under 5 years of age. Type 3 virus was isolated in 41.7% of cases, type 1 in 31.7%, and type 2 in 15.0% (Table 3). Mixtures of two types of poliovirus were present in 7 cases (11.7%): types 1 and 2 were isolated in three of these cases (42.9%), types 1 and 3 in one case (14.3%), and types 2 and 3 in three cases (42.9%).

Date of onset of paralysis

The onset of VAPP showed clear peaks during October and November 1999, when national mass immunization campaigns were held, and there were smaller peaks in January, March and December (Fig. 2). Recipient cases made up a larger proportion of the total VAPP cases in January, February, November and December. In October and March, however, recipient cases made up a small proportion of the total despite the fact that national or subnational campaigns were held in these months.

OPV doses

Of the 60 recipient VAPP cases, nine (15.0%) had received 1 dose of OPV, four (6.7%) had received 2 doses, 15 (25%) had received 3 doses, and 32 (53.3%) had received more than 3 doses (Fig. 3). The nine first-dose recipient VAPP cases were significantly younger than the remaining 51 who had received at least 2 doses (199 ± 139 days vs 749 ± 577 days, Kruskal–Wallis $P < 0.001$) but did not differ with respect to the

Table 2. **Comparison of recipient VAPP[a] cases ($n = 60$) and non-recipient VAPP cases ($n = 121$), India, 1999**

Variable	All VAPP	Recipient VAPP	Non-recipient VAPP	*P*–value
Age (days)	933 ± 844	665 ± 569	1063 ± 924	0.003
No. of OPV doses	4.5 ± 3.2	4.6 ± 3.1	4.4 ± 3.3	0.62
Asymmetric paralysis	125/178 (70.2%)[b]	41/60 (68.3%)	84/118 (71.2%)	0.83
Fever	120/178 (67.4%)	38/58 (65.5%)	82/120 (68.3%)	0.84
Age < 5 years	158/181 (87.3%)	56/60 (93.3%)	102/121 (84.3%)	0.14

Data are presented as means ± standard deviations (continuous variables) or as proportions with presence of attributes.
[a] Vaccine-associated paralytic poliomyelitis.
[b] Figures in parentheses are percentages.

Table 3. **Isolates of vaccine-related polioviruses from VAPP[a] cases, India, 1999**

	No. with an isolate	No. with:			No. with mixtures of isolates
		Type 1	Type 2	Type 3	
All VAPP	181	59 (32.6%)[b]	39 (21.5%)	60 (33.1%)	23[c] (12.7%)
All recipient VAPP	60	19 (31.7%)	9 (15.0%)	25 (41.7%)	7[d] (11.7%)
All non-recipient VAPP	121	40 (33.1%)	30 (24.8%)	35 (28.9%)	16[e] (13.2%)

[a] Vaccine-associated paralytic poliomyelitis.
[b] Figures in parentheses are percentages.
[c] Six mixtures of types 1 and 2, six of types 2 and 3, nine of types 1 and 3, two of types 1, 2 and 3.
[d] Three mixtures of types 1 and 2, three of types 2 and 3, one of types 1 and 3.
[e] Three mixtures of types 1 and 2, three of types 2 and 3, eight of types 1 and 3, two of types 1, 2 and 3.

Fig. 1. **Age distribution of VAPP cases, India, 1999**

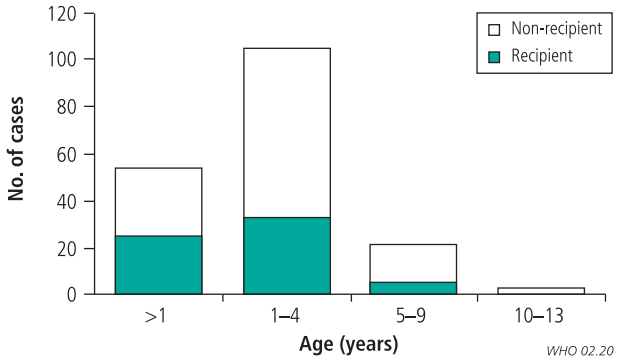
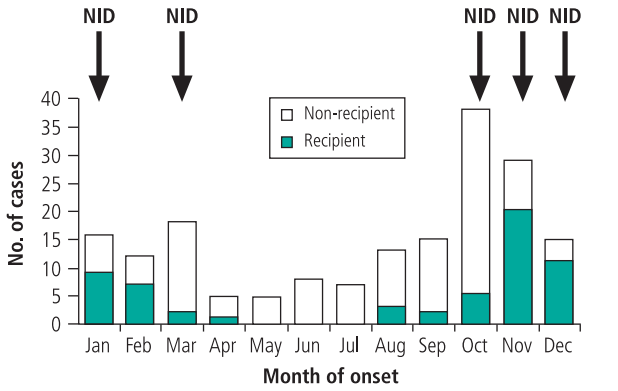
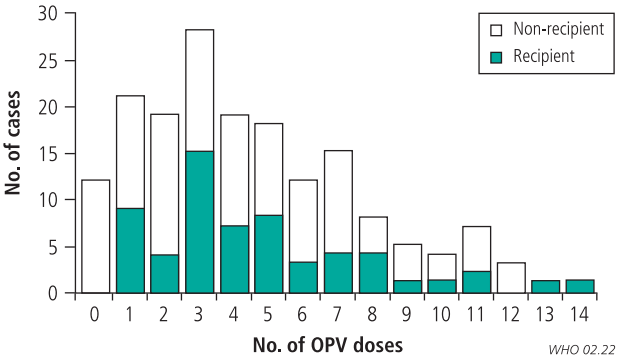


Fig. 2. **VAPP cases by month of onset, India, 1999**



NID = national immunization day.

Fig. 3. **Distribution of OPV doses received before VAPP onset, India, 1999**



presence of fever at the time of onset of paralysis, asymmetric paralysis, or isolation of the three types of poliovirus.

Estimated risk of VAPP

Table 4 shows the estimated risks of overall and recipient VAPP. The overall risk ($n = 181$) was estimated to be 1 case per 4.1 million OPV doses administered. The risk of recipient VAPP ($n = 60$) was estimated to be 1 case per 12.2 million doses administered. The risk of first-dose recipient VAPP (1 case per 2.8 million doses) was higher than the risk of subsequent-dose recipient VAPP (1 case per 13.9 million doses). The overall VAPP risk was recalculated after exclusion of (i) the 13 cases for which there was no information on the date of the last OPV dose but for which there was a record of at least one dose, and (ii) the 8 cases for which there was no information on the date of the last OPV dose and on the total number of doses received. This gave an overall VAPP risk of 1 case per 4.6 million doses administered. The risk of recipient VAPP was unchanged, as there was no information on the interval between the administration of OPV and the onset of paralysis for the 21 excluded cases.

Discussion

The results indicated that there were similarities in VAPP between India and industrialized countries, i.e. small risk, and first-dose risk higher than subsequent-dose risk. However, in India the median number of OPV doses before the onset of VAPP was higher than in industrialized countries and the children with recipient VAPP were older. The limitations of the data made it impossible to consider contact VAPP separately and to assess the contribution of provocation by injection, if any, to the VAPP risk estimates.

Despite extensive exposure to OPV during mass vaccination campaigns and in the routine immunization programme, the overall estimated risk of VAPP in India was lower than that in Latin America (1 case per 1.5–2.2 million doses administered) (*6*), England and Wales (1 case per 1.4 million doses administered) (*3*), and the USA (1 case per 2.5–3.2 million doses distributed) (*4*). In the United Kingdom and the USA, OPV has been given solely through routine health services. In Latin America, however, mass immunization campaigns were conducted in order to supplement routine immunization. The magnitude of the mass immunization campaigns in India has been unprecedented, each NID having reached at least 125 million children every year since 1996 (*17*). Exposure to OPV has thus been intense.

Table 4. **Risk of VAPP[a], India, 1999**

	Risk of:	
	Recipient VAPP	**Total VAPP**
Overall risk[b]	1/12.2 million (60)[e]	1/4.1 million (181)[e]
First-dose risk[c]	1/2.8 million (9)	–
Subsequent-dose risk[d]	1/13.9 million (51)	–

[a] Vaccine-associated paralytic poliomyelitis.
[b] Overall risk denominator is total number of OPV doses distributed over one year as routine immunization and through national mass immunization campaigns (733.4 million).
[c] First-dose risk denominator is annual birth cohort (25 million).
[d] Subsequent-dose risk denominator is total number of OPV doses distributed annually minus annual birth cohort (708.4 million).
[e] Numbers in parentheses are numbers of cases.
[f] Overall VAPP risk, excluding 21 cases with unknown OPV immunization histories, is 1 case per 4.6 million.

Table 5. **Factors potentially associated with increased or decreased VAPP[a] risk in India**

Increased VAPP risk	Decreased VAPP risk
Intense and frequent OPV exposure during national immunization days	Early exposure to wild poliovirus, resulting in type-specific immunity (protection from vaccine-related virus)
Provocation poliomyelitis (multiple injections)	Early exposure to vaccine-related virus (routine immunization at birth[b] and 6, 10, and 14 weeks)
Aggravation poliomyelitis	Increased maternally-derived antibody titerres in infants (most mothers repeatedly exposed to wild poliovirus)
	Lower OPV immunogenicity, particularly for type 3 component, in developing countries (permits P2 type-specific immunity to develop first, providing some cross-immunity to P3)

[a] Vaccine-associated paralytic poliomyelitis.
[b] Birth dose recommended for institutional births.

The somewhat lower risk of VAPP observed in India relative to estimates from Latin America, the United Kingdom, and the USA, may be attributable to several factors present in India and other countries in which polio is endemic (Table 5). First, the force of wild poliovirus infection, as measured by the average age of infection (*18*), is substantially higher than in industrialized countries. Viral exposure occurs at an earlier age, when many infants are still protected by maternally-derived antibodies, which would be expected to prevent both paralytic poliomyelitis and VAPP. Infants in India remain under the protection of maternally derived antibodies longer than those residing in industrialized countries, since mothers are likely to be exposed to wild poliovirus on many occasions. Moreover, vaccine-related virus exposure is frequent and repeated even among unvaccinated infants and children (*19*). The routine OPV immunization schedule in India is skewed towards the younger ages, which induces active immunity against polio at an early age. These factors lead to decreasing susceptibility to polio with increasing age, which is reflected by the age distribution of the disease (*2*). All of these factors would be expected to reduce the VAPP risk in countries where polio is endemic. However, as the force of wild poliovirus infection decreases the proportion of all polio cases attributable to VAPP can be expected to increase.

As expected, giving large numbers of supplemental OPV doses during mass immunization campaigns caused the estimated risk of subsequent-dose VAPP to diminish by selectively increasing the magnitude of the denominator without changing the numerator. The estimated risk of first-dose recipient VAPP was substantially higher than that of subsequent-dose recipient VAPP. However, the distribution of OPV doses given to all recipient VAPP cases showed that of the 60 recipient VAPP cases, 9 (15%) had received only 1 dose and 32 (53.3%) had received 4 or more. Of the 113 non-recipient VAPP cases for which there were data on the number of doses, 61 (54%) had received 4 or more OPV doses. This high proportion of VAPP cases that had received at least 4 doses possibly reflected lower OPV immunogenicity, which has been documented in developing countries (*9*, *20*). It is also possible that the OPV administered in India was of lower potency and that deficiencies in the cold-chain were responsible for reduced potency. Some VAPP cases in our study may not have received potent OPV until their third or fourth dose, at which point they would have been susceptible and consequently could have developed VAPP. Nevertheless, the supplementation of routine immunization with OPV doses from regular mass campaigns has markedly reduced wild poliovirus transmission in India and remains an essential strategy for eradication in all remaining countries in which polio is endemic.

Our data showed increased numbers of VAPP cases during October and November 1999 and smaller peaks during January, March and December, all months during which mass immunization campaigns were conducted. The increased numbers of VAPP cases during the winter months probably resulted from the massive amounts of OPV administered throughout the country during this season of low transmission of wild poliovirus. In each of these months, recipient VAPP cases accounted for approximately half of all VAPP cases. However, the proportion changed from March to October, when recipient VAPP cases made up only a small proportion of the total. This change may have been partly attributable to the misclassification of non-VAPP cases as VAPP cases in instances where AFP actually had other causes.

Type 1 poliovirus was isolated in a high proportion of VAPP cases. This had not been expected because of findings in other populations. The proportion of type 1 VAPP cases was similar in months when NIDs were held and in months when they were not held (31% and 35.4% respectively of all VAPP cases; 31.9% and 30.8% respectively of all recipient VAPP cases). With the exception of three cases of VAPP involving type 1 poliovirus in a district of Uttar Pradesh where onset began on 5–9 November, there was no apparent temporal or geographical clustering. Similar results emerged from a previous study (*6*) in which type 3 was the most common serotype, occurring in 50% of recipient VAPP cases, while type 1 occurred in 34.6%. In our recipient VAPP cases, type 3 was isolated most frequently (48.3%), followed by type 1 (38.3%). It is important to note that while type 1 poliovirus was frequently isolated in our VAPP cases, we used a conservative case definition and thus some of these type 1 cases may not have been cases of true VAPP.

The Indian AFP surveillance system is primarily a tool for monitoring progress in the eradication of wild poliovirus transmission. It is not designed to collect comprehensive data for the assessment of VAPP risk. The misclassification of cases may have resulted from incomplete detection of either wild or vaccine poliovirus, incomplete vaccination histories, and inaccurate assessment of residual paralysis. OPV-derived virus isolated in the stools of AFP cases with other causes is expected and is not proof of a causative link between paralysis and vaccine use. A subset of the VAPP cases identified for these analyses had final diagnoses suggesting that they were unlikely to be true VAPP cases, e.g. Guillain-Barré syndrome. However, the data from the surveillance system were not complete and it was not possible to exclude any presumptive VAPP cases that had probable non-polio final diagnoses at 60-day follow-up. As a result, the inclusion of these cases may have led to an overestimation of the VAPP risk. The most accurate risk estimates in this analysis are those relating to recipient VAPP, particularly first-dose recipient VAPP, for which comparisons between studies in different countries are most easily made.

At least one stool specimen was collected from 92.7% of the 9576 AFP cases with onset of paralysis in 1999, and two were collected from 90.7% of them. Two adequate stool samples were collected within 14 days of the onset of paralysis for 6739 (70.4%) of the reported AFP cases. The case definition required isolation of vaccine-related virus in at least one stool sample and the lack of wild poliovirus in any stool sample. However, no constraints were placed on the number of adequate stool samples required. It is possible that VAPP cases were missed because either no stool samples were collected, inadequate samples were collected and testing could not be done, or only one sample was collected and tested negative for vaccine-related virus. Similarly, it is possible that wild virus was not detected in cases with inadequate stool samples. All WHO network polio laboratories in India meet WHO accreditation criteria and stool samples are carried by hand from the field to laboratories in order to minimize transit time and maintain the reverse cold chain. Inadequate specimens are thus not likely to result from reverse cold chain failure or laboratory error, and the misclassification of viral isolation results is likely to be minimal, particularly when two adequate stool samples are obtained. It should be noted that the overall stool collection rate in India during 1999 was similar to that in the sample used to estimate VAPP risk in the USA. At least one stool specimen was taken for poliovirus isolation within 14 days of the onset of paralysis from 57 (71.3%) of the 80 VAPP cases meeting the case definition in the USA in 1980–89 (*4*). However, our VAPP case definition, which required the isolation of vaccine-related virus, was more specific than that used in the USA, where the isolation of vaccine-related virus was not required. It is possible that we missed some VAPP cases because of missing data (inadequate stool samples); the result of this would have been to underestimate the VAPP risk.

Several assumptions were made in estimating the denominators for risk calculations. During NIDs, immunization booths may erroneously report the number of OPV doses administered on the basis of the number of empty OPV vials at the end of the day rather than on the number of doses administered. This may have contributed to our estimated VAPP risk being lower than the values obtained in Latin America and the United Kingdom. Furthermore, it is difficult to determine accurately the denominator for subsequent-dose recipient VAPP, particularly in countries such as India where extremely large numbers of children are immunized during mass immunization campaigns at least twice a year. We could not differentiate between VAPP associated with routine immunization doses and that associated with mass campaigns, as these data were not collected by the surveillance system. Additionally, it was not possible to conduct a more detailed examination of the VAPP cases in order to determine whether they had typical polio paralysis at 60-day follow-up or whether they had recovered at a later time. It was therefore likely that non-VAPP cases were included in the analyses and that the estimated VAPP risks were thus inflated.

The data from the AFP surveillance system in India show a lower risk of VAPP than in other populations, despite intense and repeated exposure to many more doses of OPV than in industrialized countries. These findings in a tropical developing country where polio is endemic are particularly significant since wild poliovirus transmission is rapidly decreasing in India and in other countries where the disease is endemic, and where providers and parents are increasingly concerned about VAPP. The risk of paralytic disease from wild poliovirus infection still far outweighs the risk of VAPP in countries where polio is endemic, and experience has shown that OPV, particularly when distributed in mass campaigns, is an essential tool for rapidly raising herd immunity and interrupting wild poliovirus transmission. The results of this analysis and of analyses from other populations indicate that the risk of VAPP remains quite small even when OPV is administered to large numbers of children through mass immunization campaigns. Efforts should therefore be intensified with a view to achieving the goal of global polio eradication by the end of 2002 and the subsequent discontinuation of OPV vaccination to ensure that no child will ever again experience paralytic disease, disability and death associated with either wild poliovirus or vaccine-related poliovirus. ■

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Conflicts of interest: none declared.

Résumé

Poliomyélite paralytique associée à la vaccination en Inde pendant l'année 1999 : diminution du risque malgré l'utilisation massive du vaccin oral

Objectif La poliomyélite paralytique associée à la vaccination (PPAV) est une conséquence rare mais grave de l'administration de vaccin antipoliomyélitique oral (VPO). L'intensification de la vaccination par le VPO a réduit la transmission du poliovirus sauvage en Inde mais la PPAV devient un sujet de préoccupation.

Méthodes Nous avons analysé les données de surveillance concernant la paralysie flasque aiguë (PFA) afin d'estimer le risque de PPAV dans ce pays. La PPAV a été définie comme poliomyélite paralytique observée parmi les cas de PFA avec début de la paralysie en 1999, faiblesse musculaire résiduelle 60 jours après le début de la paralysie et isolement d'un poliovirus de type vaccinal. Les cas de PPAV chez les sujets récemment vaccinés constituaient un sous-ensemble de cas chez lesquels la paralysie débutait entre 4 et 40 jours après l'administration du VPO.

Résultats Au total, 181 cas de PFA répondaient à la définition de cas de PPAV. Les estimations de risque suivantes ont été faites : risque global, 1 cas pour 4,1 à 4,6 millions de doses de VPO administrées ; risque chez les sujets récemment vaccinés, 1 cas pour 12,2 millions ; risque chez les sujets ayant récemment reçu la première dose de vaccin, 1 cas pour 2,8 millions ; risque chez les sujets ayant récemment reçu une dose ultérieure de vaccin, 1 cas pour 13,9 millions.

Conclusion Le risque estimé de VAPP en Inde, calculé d'après les données d'un système de surveillance très sensible, est à l'évidence plus faible que dans d'autres pays, malgré l'administration de doses multiples de VPO aux enfants dans le cadre de campagnes de vaccination de masse.

Resumen

Poliomielitis paralítica de origen vacunal en la India durante 1999: reducción del riesgo pese al uso masivo de la vacuna antipoliomielítica oral

Objetivo La poliomielitis paralítica de origen vacunal (PPV) es una consecuencia infrecuente pero grave de la administración de la vacuna antipoliomielítica oral (OPV). La intensificación de la administración de OPV ha reducido la transmisión del poliovirus natural en la India, pero la PPV está empezando a suscitar preocupación.

Métodos Analizamos los datos de vigilancia de la parálisis fláccida aguda (PFA) a fin de estimar el riesgo de PPV en el país. Se estableció que debían considerarse PPV los casos de PFA con inicio de la parálisis en 1999, debilidad residual 60 días después del comienzo de las manifestaciones, y aislamiento del poliovirus vacunal. Los casos de PPV de receptores se identificaron con el subgrupo en el que la parálisis se había iniciado entre 4 y 40 días después de la administración de OPV.

Resultados En total, 181 casos de PFA satisficieron la definición de caso. Se hicieron las siguientes estimaciones del riesgo de PPV: riesgo global, 1 caso por 4,1–4,6 millones de dosis de OPV administradas; riesgo de receptor, 1 caso por 12,2 millones; riesgo de receptor de primera dosis, 1 caso por 2,8 millones; y riesgo de receptor de dosis subsiguientes, 1 caso por 13,9 millones.

Conclusión A juzgar por los datos suministrados por un sistema de vigilancia altamente sensible, el riesgo estimado de PPV en la India es claramente menor que el correspondiente a otros países, pese a la administración de múltiples dosis de OPV a los niños durante las campañas de inmunización masiva.

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