Why have we failed to eradicate polio from India?

Yash Paul, MB;BS, DCH
Consultant Pediatrician,
A-D-7, Devi Marg
Bani Park
Jaipur-302 016, India.
Phone: 91-141-2314774
Email: dryashpaul2003@yahoo.com

Abstract

Polio eradication is a national program in India. The Government of India through the Health Department along with the Health Departments from all the states of the country and UNICEF, supported by Rotary International and the Indian Academy of Pediatrics is conducting AFP surveillance and providing Oral Polio Vaccination (OPV). Millions of Indians are involved in this program.

OPV has successfully eradicated polio from many parts of the world, but, it has failed to eradicate polio from India, though the deadline for polio eradication was extended from 2000 to 2002. The vaccine has failed to provide protection to many children who have developed paralytic polio even after taking ten or more doses of OPV. In some children OPV has caused paralysis--vaccine associated paralytic polio (VAPP). The number of children developing polio due to vaccine is unacceptably high. As inactivated polio vaccine (IPV) is not available, even immunocompromised children are being administered OPV, adding to the high number of VAPP cases. Because of non-availability of IPV and poor potency OPV, polio cases will continue to occur and polio will not be eradicated from India.

Keywords: Polio eradication, vaccine failure, vaccine associated paralytic poliomyelitis (VAPP)

1. Introduction

OPV has successfully eradicated polio from many parts of the world, but, it has failed to eradicate polio from India. Deadline for polio eradication had been shifted from the year 2000 to the year 2002. During the year 2001 very low incidence of polio had been reported from all over the country, and it was hoped that polio would be eradicated from India by the end of 2002. But, during the year 2002 wild polioviruses had been reported in large number of cases from many parts of the country, even from those parts which had not reported polio incidence for some years. The number of cases of poliomyelitis caused by wild polioviruses in India had declined from 1126 in 1999 to 265 in 2000 and 268 in 2001. Reversing this trend, there were 1509 cases during 2002, accounting for over 87% of cases detected globally [1]. Later number of virologically confirmed cases in India rose to 1600.

The experts reassured, "In all probability we may achieve the elimination of wild viruses in India within a short time, perhaps in 2003 itself [2]. As on 29th November 2003, wild polio viruses had been detected in 194 cases; but as on 28th February 2004, wild polio viruses had been detected in 225 cases, with 402 pending cases for the year 2003.

One expert had stated: "The number of districts with polio had declined to 63 in 11 states in 2001, but in 2002 cases occurred in 146 districts in 16 states. Kerala, Tamil Nadu, Andhra Pradesh and Karnataka remained unaffected; in these states, routine and pulse immunizations have remained robust through the years [3]." But during the year 2003, wild polioviruses emerged in Tamil Nadu, Andhra Pradesh and Karnataka.

The resurgence of wild polioviruses, especially in those parts of the country where polio had not been reported for some years showed that there had been some deficiencies in the vaccine and/or the strategy. All those associated with polio eradication program believe that failure to eradicate polio was only because of lack of 100% vaccine coverage. This presumption is incorrect, because in that case only unvaccinated and partially vaccinated children should have developed polio, and no fully vaccinated children would have developed polio.

2. The vaccine : Oral Polio Vaccine (OPV)

2.1 Attenuated vaccine polioviruses replicate and multiply in the gut of the vaccinees and may generate antibodies resulting in immunity. The vaccine genotypes are unstable and vaccine viruses may, and usually do, backmutate quite often to increasing neurovirulence during multiplication in the human host [4]. Attenuated vaccine polioviruses are markedly reduced in neurovirulence but also have decreased infectivity through secondary spread resulting in infrequent transmission from vaccinated children to contacts [5]. If both neurovirulence and transmissibility are acquired by the vaccine strain, then the resultant mutant virus is virtually wild-like, called Vaccine-derived Wild-like (VDWL), also called revertants [6].

2.2 OPV dynamics

When OPV is administered to a non-immune individual, one or more of the following can occur:

a. Immunity

Antibodies may form providing protection against that specific serotype(s).

b. Herd Immunity

The attenuated vaccine polioviruses shed in feces of those vaccinated and infect non-immune individuals through secondary spread. These secondarily infected individuals may form antibodies and develop immunity without directly taking the vaccine.

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c. Herd protection

The immunized persons may provide protection to a non-immune individual without inducing immunity, essentially by breaking the transmission of the infection or lessening the chances of a susceptible coming in contact with an infected individual [7].

d. Recipient VAPP

Revertant neurovirulent vaccine polioviruses in OPV may cause paralytic polio in the vaccine recipient. This is called vaccine associated paralytic poliomyelitis (VAPP).

e. Contact VAPP

Revertant neurovirulent vaccine polioviruses shed in the feces by the vaccine recipient may cause paralysis in non-immune individuals.

f. Vaccine failure

The vaccine fails to generate sufficient antibodies to provide protection against paralysis.

The latter three, namely recipient VAPP, contact VAPP and vaccine failure have negative impact on polio eradication. Thus the outcome of vaccination depends on which of the above mentioned six events have occurred predominantly. The additional benefit of OPV, namely herd immunity due to secondary spread of vaccine viruses, occurs rarely. As already stated attenuated vaccine polioviruses have reduced transmissibility through secondary spread, so few vaccine polioviruses infect the contacts. One dose of two drops of OPV contains about 1,000,000 vaccine polioviruses of serotype 1, about 100,000 vaccine polioviruses of serotype 2, and about 600,000 vaccine polioviruses of serotype 3, i.e., about 1,700,000 vaccine polioviruses in each dose. One gram of stool contains about 100 vaccine polioviruses [8], i.e., 17 Kg of fecal matter contain the same quantity of vaccine polioviruses that are contained in one dose of OPV. How much antibody generation is likely to occur by the few thousand vaccine polioviruses reaching non-immune child by the secondary spread when many doses of OPV are known to have failed to provide protection to many children? Similarly the children who do not develop immunity following OPV administration may continue to participate in multiplication and transmission of wild polioviruses. A vaccine which does not provide protection to many recipients will provide poor herd protection.

2.3 Vaccine failure

Vaccine failure with OPV can occur due to presence of some inhibitors in the intestinal tract of the children or due to poor quality of the vaccine. The potency of the vaccine can be affected during manufacture, transportation or storage. Many studies from India have shown that there is high incidence of vaccine failure [8]. Kohler et al had stated that it was also possible that the OPV administered in India was of lower potency and that the deficiencies in the cold chain were responsible for reduced potency [9].

In a study from a Sentinel Center for 1989 to 1994 period, it was reported that the number of children who developed paralytic polio after being fully immunized with three or more doses was 14% in 1989 and increased to 22.9% in 1994 [10]. In Rajasthan the number of children who had received five or more doses of OPV before onset of paralysis was 18/56 (32.1%) in 1999 [11] and 34/58 (58.6%) in 2000 [12]. Out of 181 VAPP cases from India during 1999, 78 children had received five or more doses of OPV before onset of paralysis [9]. Vaccine failure leaves the vaccine recipient non-immune, thus vulnerable to paralytic attack by wild polioviruses as well as by neurovirulent revertant vaccine polioviruses. Such children continue to participate in wild poliovirus circulation.

3. **The Strategy**

3.1 **Non availability of IPV (inactivated polio vaccine)**

IPV does not cause VAPP. Risk of VAPP with OPV is more in immunocompromised individuals, whether due to disease or drugs. As IPV is not available in India the doctors have two options: (i) not to administer OPV to these children and leave them vulnerable to wild poliovirus infection or (ii) administer OPV to these children and expose them to the risk of VAPP which is very high for these children.

3.2 **Immunocompromised child**

As stated already these children are at higher risk to develop VAPP, and because of immunocompromised state, are more vulnerable to any infection, including that by wild polioviruses. Wild polioviruses replicate, multiply and are shed for prolonged periods, sometimes for many months or years in immunocompromised individuals, thus such individuals pose high risk for the community.

4. Outcome

4.1 Vaccine failure and high incidence of VAPP

Vaccine failure leaves the child non-immune and vulnerable to paralytic attack by wild polioviruses as well as well as by neurovirulent revertant vaccine polioviruses. Through secondary spread, contacts of the vaccinee would receive both attenuated as well as neurovirulent vaccine polioviruses, as shown in figure 1. Attenuated vaccine polioviruses can cause immunity in the non-immune contact, but as already mentioned it occurs rarely. Neurovirulent revertant vaccine polioviruses can cause VAPP in non-immune contact as already mentioned because of increased virulence and transmissibility.

OPV used for routine vaccination and mass vaccination called pulse polio immunization (PPI) is the same, but is administered for different reasons. The vaccine, whether given to children on different days (routine vaccination) or administered to all of those eligible on same day (PPI), is primarily for providing immunity to the recipients. When all susceptible children are administered OPV simultaneously, both attenuated and mutant vaccine polioviruses would be excreted in feces, and through secondary spread reach other children including vaccine recipients. During simultaneous administration if all the children develop immunity, there would be no risk of VAPP by secondary spread of mutant neurovirulent vaccine polioviruses, as shown in figure 2. Mass vaccination or PPI is done to prevent adverse effects of secondary spread of mutant vaccine polioviruses. If there is vaccine failure due to any reason, then those children who do not develop immunity may develop VAPP even during the mass vaccination campaigns. This is the reason that the incidence of VAPP in India is higher than the

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expected incidence [11,12]. The expected number of VAPP cases per year was 60-75 [13], but in a study by Kohler et al there were 181 VAPP cases during 1999 [9].

It may be relevant to state that (i) Kohler et al had not included those children who had developed paralysis four to forty days after taking OPV, but vaccine polioviruses had not been detected in the stool samples, and (ii) AFP surveillance is done for individuals up to the age of fifteen years, those above fifteen years of age who had developed contact VAPP remain unknown to the Surveillance Medical Officers. Thus number of VAPP cases which had occurred during 1999 was higher than 181. (During 1999, 9587 individuals aged <15 years were reported to have developed acute flaccid paralysis, 1126 were virologically confirmed polio cases, 181 cases had developed polio due to OPV.)

Dr. Jacob John had stated: "As long as immunity levels are maintained high with early vaccination of all children, the risk of infection by vaccine derived neurovirulent mutants will remain low. However, if vaccination slackens, then the risk of infection from environmental source may increase [3]. He had further stated: "Maintaining high levels of immunity through vaccination is essential to preempt such occurrence. Immunization with OPV protects from wild and VDWL viruses; continued high coverage prevents the emergence of VDWL" [3]. But this benefit occurs with potent vaccine only.

4.2 VAPP after subsequent OPV dose

It is stated that VAPP occurs most frequently after the first OPV dose. The risk of VAPP is not equal for all OPV doses in the vaccination series. The risk of VAPP is 7-21 times higher for the first dose than any other dose in the OPV series. The reason for this difference by dose is not known with certainty, but is probably because the vaccine virus is able to replicate longer in a completely non-immune infant. This prolonged replication increases the chance of the emergence of a revertant virus that may cause paralysis. The situation is similar for contacts. A non-immune child may shed virus longer, increasing the chance of exposure to contact [14]. Out of 181 VAPP cases from India during 1999, 78 children had received five or more doses of OPV before onset of paralysis [9]. Thus it can be stated that the effective OPV dose, be it the first or the tenth dose administered, may cause VAPP. Because of high incidence of vaccine failure in India, the majority of VAPP cases occur after a subsequent OPV dose. In the study by Kohler et al [9], out of sixty recipient VAPP cases, only nine had developed VAPP after first dose.

5. Conclusions

The agencies involved in polio eradication from India attribute 'failure to vaccinate all', and not 'vaccine failure' as the reason for failure of the program. The fact that (1) many children have developed polio in spite of many doses of OPV and (2) some have developed polio because of the vaccine (VAPP) suggests that OPV may at the most result in decreased incidence of polio but can not eradicate polio. Rather it can be stated that the present eradication program ensures that polio will not be eradicated as polio cases will continue to occur because of vaccine failure as well as because of the vaccine.

It is suggested that the following measures be taken urgently: (1) IPV be made available for those children who are immunocompromised or have immunocompromised close contacts and (2) the reason(s) for vaccine failure be determined and appropriate remedial measures, if feasible be taken. Otherwise some alternate strategy for polio eradication should be formulated.

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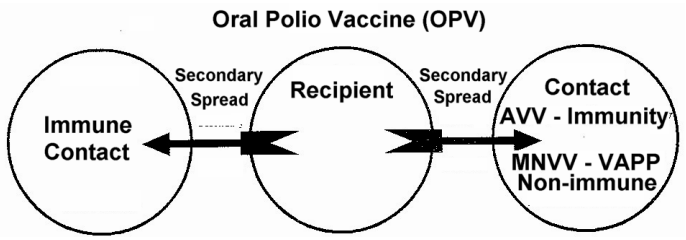
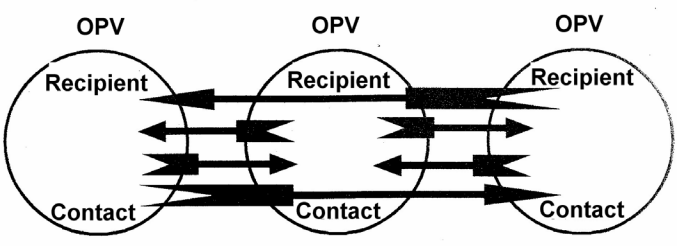
Figure 1. Routine Immunization



AVV – attenuated vaccine virus
MNVV – mutant neurovirulent (neurovirulent revertant) vaccine virus
VAPP – vaccine associated paralytic polio

Figure 2. Mass Immunization



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