Polio Eradication in India: Need to Switch over to IPV from OPV

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Abstract

Vaccines have reduced the prevalence of preventable infectious diseases to a minimum level. Small pox and polio are the best examples. Vaccines could be live vaccine or inactivated vaccines. However none of these are absolutely safe. India achieved a major milestone in 2012 with the World Health Organization striking it off the list of polio endemic countries on 25 February 2012, after India completed one year without any case of polio. As the goal of wild poliovirus eradication is approached, concern has been raised about the potential for persistent transmission of oral polio vaccine (OPV) viruses, as these viruses are known to revert toward wild-type neurovirulence. The phenotypic reversion of the OPV strains to neurovirulence is thought to be the underlying mechanism for the reported cases of vaccine-associated paralytic poliomyelitis among OPV recipients or their close contacts. However, cases of VAPP have not been reported with the use of inactivated polio vaccine. The “endgame” for worldwide poliomyelitis eradication will require stepwise cessation of the use of oral poliovirus vaccine (OPV) for various strains in all countries and finally to switch over to IPV to prevent the danger of vaccine-derived polioviruses—exposing some populations to risk of poliovirus outbreaks.

Keywords: Vaccines, Polio Immunization, Oral Polio Vaccine, Inactivated Polio Vaccine, Vaccine Associated Polio Paralysis
INTRODUCTION

Effective control measures can lead to decrease in the incidence of certain infectious diseases that affect human and animal health. Vaccination has successfully interrupted circulation of poliomyelitis, measles, and rubella and has drastically reduced the incidence of diseases affected by these pathogens. However, despite these successes, eradication of established pathogens has been limited to only one human (smallpox) and one animal (rinderpest) diseases.

Vaccination against polio in 1955, in the the form of inactivated polio vaccine (IPV) and later live oral polio vaccine (OPV)) IN 1962 led to immense reductions in the burden of poliomyelitis disease in most of the countries leaving behind only three Pakistan, Afghanistan and Nigeria affected by endemic poliomyelitis.

The global eradication program had emphasized the use of OPV due to its low cost and relative ease of its administration, as compared with IPV. Furthermore, OPV viruses can be transmitted from vaccinees to their contacts, which results in immunization of some individuals who may be missed by a vaccination program. The problem facing the Polio Eradication Initiative is whether OPV viruses could persist as naturally acquired and transmitted infections in human populations, after cessation of vaccination. However, OPV can also cause – in rare instances – paralytic polio cases. Polio cases due to vaccine-associated paralytic poliomyelitis (VAPP) and outbreaks due to circulating vaccine-derived polioviruses (cVDPVs), are the two main reasons for eventually stopping the use of OPV for routine immunization in all countries. Once eradication of wild poliovirus has been confirmed, the public health benefits of routine immunization with OPV will no longer outweigh the burden of disease due to VAPP and cVDPVs.

POLIO AND ERADICATION CAMPAIGN

Poliomyelitis, an infectious disease with acute and persistent flaccid paralysis is caused by poliovirus (types 1, 2 or 3), an enterovirus. Up to 95% of all polio infections are inapparent or subclinical. Estimates of the ratio of inapparent to paralytic illness vary from 50:1 to 1,000:1 (usually 200:1).

The Global Polio Eradication Initiative was launched in 1988 with the aim to eliminate paralytic poliomyelitis. The World Health Organization (WHO) was encouraged to commit to the eradication of poliomyelitis from the world by 2000. By 2000, the estimated number of polio cases worldwide had declined 99 per cent from 1988 but failed to meet this target, by the end of 2000 in Indian subcontinent and central Africa. The whole of the Pacific region including most of South-East Asia and America and China were free of this disease.

National Immunization Days (NIDs) played a major role in eradication, the aim being to immunize all children under the age of 5 years in a region or country, ideally in a single day. India had regularly immunized 120 million children at a time, with immunization events occurring every other month. Usually two or three rounds of vaccination supplemented by mopping-up programmes, and sub-NIDs (SNIDs) in limited areas were sufficient to keep the virus under control. In fact, there were several examples where wild-type virus continued to be found in sewage. This had raised questions...
about the eradication of wild type virus. Reliable surveillance to identify cases was essential.\textsuperscript{10}

In India The last polio case was reported on January 13, 2011 from the state of West Bengal, and was a case of wild polio virus-1 (WPV 1). The virus has not been detected in sewage samples during this period in India. India must sustain this feat of zero new case for another 2 years to be declared “polio-free.” \textsuperscript{10,11}

**POLIO VACCINES AND VACCINE DERIVED POLIO VIRUS**

There are two types of vaccines currently in use for polio vaccination, namely, oral polio vaccine (OPV) and inactivated polio vaccine (IPV). The Salk ‘inactivated polio vaccine’ (IPV) contains all three types of poliovirus killed by treatment with formaldehyde. It elicits protective antibodies in the blood that stop wild type virus infection spreading from the gut to the central nervous system. IPV therefore provides excellent individual protection against paralytic polio. \textsuperscript{12}

The Sabin OPV contains live attenuated virus (all three types), is easily swallowed and yet does not cause disease. OPV confers strong gut immunity that limits wild virus multiplication and reduces its spread from person to person. For a few months, OPV virus is shed into the stools of recently immunised children, and in areas where hygiene and sanitation are inadequate this can result in immunisation of close contacts. OPV is cheaper, easier to administer as drops by mouth, and can be given by volunteers without the need for healthcare workers, needles, or syringes. \textsuperscript{12,13}

OPV contains attenuated polio viruses from the three principal polio strains (named 1, 2 and 3). Immunity to one of these types does not provide immunity to the other two. An attenuated vaccine contains live but weakened virus with reduced infectivity. Three doses of OPV are recommended, but as a result of NIDs, SNIDs and the ‘mop up’ campaigns, some children may receive ten or more doses in endemic areas. However, the vaccine virus genotypes are themselves unstable and during multiplication in the human host, frequently backmutate, often resulting in increased neurovirulence. These mutations are known as vaccine-derived wild-like polioviruses (VDWL viruses). Clinical disease, including paralysis, caused by vaccine-derived poliovirus (VDPV) is indistinguishable from that caused by wild polioviruses. In areas where OPV is used contact with VDWL viruses is common because both the attenuated OPV polioviruses and the VDWL polioviruses may be shed in the faeces after vaccination. Transfer can then occur among individuals through the faecal-oral route. Contact with these polioviruses has both potentially beneficial and harmful effects. First, these attenuated vaccine-derived polioviruses may, beneficially, stimulate antibodies in third-parties. This phenomenon is known as herd immunity. However, contact with VDWL viruses can be harmful. Mutations can cause paralysis in both the vaccine recipients and third parties: so-called vaccine associated paralytic poliomyelitis (VAPP). VAPP is a well known consequence of the use of OPV. \textsuperscript{14,15}

As the incidence of wild polio diminishes, nations transition from use of the oral vaccine back to the injected vaccine because the direct risk of iatrogenic
polio (VAPP) due to OPV outweighs the indirect benefit of immunization via subclinical transmission of OPV. The use of OPV was discontinued in the United States in 2000 and in 2004 in the UK, but it continues to be used around the globe. A nine-month-old boy from Navi Mumbai tested positive for Vaccine-Derived Poliovirus (VDPV) type 2 making it fourth such case recorded in India in 2013.15,16

**CHALLENGE TO THE ERADICATION OF ALL POLIOVIRUSES: VACCINE ASSOCIATED PARALYTIC POLIOMYELITIS IN INDIA**

Vaccine Associated Paralytic Poliomyelitis (VAPP), although a known hazard with Oral Polio Vaccine (OPV), has not received adequate attention in India despite increasing use of OPV in repeated rounds of national immunization days.

The incidence of VAPP in India is likely to be 1 in 1.5–2.0 million doses, which is higher than that reported elsewhere. The incidence of non-polio Acute Flaccid Paralysis (AFP) in India is now 12 times higher than expected and coincides with huge increases in OPV doses being given to children in the quest to “eradicate” wild type polio infection and paralysis.415,17

The rate of vaccine-associated paralytic poliomyelitis (VAPP) varies by region but is generally about 1 case per 750,000 vaccine recipients. VAPP is more likely to occur in adults than in children. In immunodeficient children, the risk of VAPP is almost 7,000 times higher, particularly for persons with B-lymphocyte disorders (e.g., agammaglobulinemia and hypogammaglobulinemia), which reduce the synthesis of protective antibodies.18,19

The National Polio Surveillance Project data show that the polio eradication program has increased paralysis among children—from 3,047 cases yearly in 1997 to 61,038 cases in 2012, most now being classified as AFP instead of polio.19

**POST-ERADICATION END GAME STRATEGIES**

Eradication will be declared when 3 years have elapsed since isolation of the last wild-type poliovirus, and laboratory production strains must be contained. There has been substantial effort in all regions to identify laboratories that have poliovirus and, as far as possible, reduce their number. But there are many hurdles for successful eradication. Firstly, wild-type virus may not have been eradicated, despite failure to detect it for 3 years; secondly, containment may not be perfect; and thirdly, the vaccine-derived viruses will certainly be present.20

At this juncture, the continued use of trivalent Oral Polio Vaccine (tOPV) in the polio eradication program poses the risk of paralysis from type 2 circulating Vaccine Derived Polio Virus (cVDPV). The Sabin type 2 in the tOPV has been responsible for >90% of all cVDPV cases and about 40% cases of VAPP globally during the last few years. All countries will continue to face the risk of type 2 cVDPV as long as tOPV is being used in the program. In order to mitigate this risk, it is important to discontinue tOPV and switch to bivalent OPV (bOPV) in both routine immunization and special immunization rounds as a part of the global ‘polio end game’ strategy. The
global Scientific Advisory Group of Experts (SAGE) on Immunization (2012) and the India Expert Advisory Group (IEAG) for polio eradication (2013) have recommended the introduction of Inactivated Poliovirus Vaccine (IPV) in the routine immunization program prior to this switch. Comparison of the immunogenicity of bOPV and IPV in the routine immunization (RI) schedule would help us to assess the immunity profile that would exist after the tOPV-bOPV switch.\(^{21}\)

Over the last 10 years, all member states of the European Union have changed independently to the use of IPV in preference to OPV, at least partly because of the cost of vaccine-associated cases. The whole of the North American continent now uses IPV exclusively, and Mexico and Russia have recently changed to IPV from OPV. It is conceivable that good global routine immunization programmes delivering a combination vaccine of which IPV is a part could provide insurance for the post-eradication era.\(^{22, 23}\)

**DISCUSSION**

The global incidence of poliomyelitis has dropped by more than 99 per cent since the governments of the world committed to eradication in 1988. One of the three serotypes of wild poliovirus has been eradicated and the remaining two serotypes are limited to just a small number of endemic regions. However, the Global Polio Eradication Initiative (GPEI) has faced a number of challenges in eradicating the last 1 per cent of wild-virus transmission. There are some major challenges to wild poliovirus eradication, focusing on the poor immunogenicity of OPV in lower-income countries, the inherent limitations to the sensitivity and specificity of surveillance, the international spread of poliovirus and resulting outbreaks, and the potential significance of waning intestinal immunity induced by OPV. In particular, with the increasing use of monovalent and bivalent OPVs against serotypes 1 and 3, gaps in population immunity to serotype 2 can lead to increasing incidence of poliomyelitis caused by circulating serotype 2 VDPVs. The polio endgame strategy addresses this challenge by calling for global, coordinated withdrawal of OPV serotypes, and eventually of all OPV. A clear strategy for the management of post-OPV risks should be clearly made including continued AFP surveillance, the maintenance of an international monovalent OPV stockpile and policy guidance on routine immunization with IPV to mitigate risks following a poliovirus re-emergence.

The successful reduction of the global incidence of poliomyelitis from over 1000 cases a day in 1988 to less than one a day in 2012 is a major achievement of the GPEI. The endgame strategy is designed to take the world from low incidence to no incidence. There is every reason to believe that this is possible with the continued commitment of the global health community.

**CONCLUSION**

Oral polio vaccines (OPV) contain live, weakened virus, which can – on very rare occasions – revert to a paralytic form and regain the ability to circulate. Replacing OPV with inactivated polio vaccines (IPV), which carry no risk of paralysis, is necessary to ensure a polio free world. The future plan will include a staged approach to complete this switch, which will include phasing out the different types of
OPV and introducing IPV into routine immunization programs.

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