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PEDIATRICS

SPECIAL VOLUME 27





Recent Advances in PEDIATRICS

Infectious Diseases II

The most up-to-date compendium of peer-reviewed, evidence-based and state-of-the-art topical issues of special relevance and applicability to the Indian subcontinent and other resource-limited countries, especially in the South-East Asian Region (SEAR)

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2 Polio Vaccines

Suraj Gupte, Shefalli Koul, Novy Gupte

ABSTRACT

Caused by an RNA enterovirus, poliomyelitis, until recently, was the most common cause of physical disability and handicap in the resource-limited countries. Characterized by clinical manifestations varying from nil to rapid paralysis, the etiologic virus has 3 strains. Type 1 strain (Burnhide) caused large epidemics, type 2 (Lansing) isolated cases and small outbreaks, and type 3 (Leon) small epidemics. Asymptomatic (silent, inapparent), abortive, nonparalytic and paralytic (spinal, bulbar, bulbospinal, or encephalitic) forms were known. Two types of polio vaccines are available: oral polio vaccine (OPV) which may further be trivalent, bivalent of monovalent, and IPV. Contrary to the earlier understanding, it is the IPV that has a better herd effect. Rarely, OPV may cause vaccine-related paralysis. Consequent upon the Global Polio Eradication Initiative, employing polio vaccine as a part of basic immunization plus pulse polio campaign, effective surveillance system and mopping up by door-to-door immunization, the disease is close to elimination/ eradication. Now that India has been polio-free over more than a three years. WHO has already declared that polio stands eradicated from India. Now, time has come for shift from all OPV to sequential OPV- IPV schedules. Subsequently, it shall be "all IPV" schedules as has been the case with the Western countries.

Keywords: Acute flaccid paralysis (AFP), Bivalent OPV, Enhanced inactivated polio vaccine (eIPV), Goodbye to polio, Inactivated polio vaccine (IPV), Monovalent OPV, Oral polio vaccine (OPV), Poliomyelitis, Polio eradication, Trivalent OPV, Sabin strain, Salk strain, Vaccine-associated polio paralysis (VAPP), Vaccine-acquired polio viruses (APV).

INTRODUCTION

Poliomyelitis, exclusively a human disease, is an acute viral infection (RNA enterovirus) characterized by clinical manifestations varying from nil to rapid paralysis. Type 1 strain (Burnhide) causes large epidemics, type 2 (Lansing) isolated cases and small outbreaks, and type 3 (Leon) small epidemics. Asymptomatic (silent, inapparent), abortive, nonparalytic and paralytic (spinal, bulbar, bulbospinal or encephalitic) forms are known.

Thanks to the international war against poliomyelitis spearheaded by the Global Polio Eradication Initiative, employing polio vaccine as a part of

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basic immunization plus pulse polio campaign, effective surveillance system, and mopping up by door-to-door immunization, the disease is close to elimination/eradication. Until recently, only four countries (India, Pakistan, Nigeria, and Afghanistan) remained to be yet polio-free. In India since 13 January 2011, no case of polio has been seen. Having already completed a minimal of 3 years (Nov 2010–Nov 2013) of polio-free India, WHO declaration that polio stands eradicated from India has become a reality. For a country that was once dubbed as the world's epicenter of polio, it is a commendable achievement.

Since India has now been taken off the list of polio endemic nations, sequential OPV-IPV approach has started. Eventually, it shall be "all IPV".

POLIO VACCINES: A–Z BASICS

Oral Polio Vaccine (OPV)[1-4]

OPV has a shelf-life of 2 years at a temperature of –20°C, 6 months at 2–8°C and 1–3 days at room temperature. As per recommendations, OPV should be stored at –20°C at the state and district level and in the freezer at the clinic level. The vaccine must reach the outreach facility at 2–8°C in vaccine carriers with ice packs. Following multiple freeze thaw cycles, the virus loses its potency. After thawing, it should be kept at temperatures between 2°C and 8°C for a maximum of 6 months.

Over the years, attaching vaccine vial monitor (VVM) has become mandatory to follow its journey through time-temperature sequences. The VVM shows a change to dark color if the vial goes through unacceptable time-temperature exposure. Once this happens, the vaccine has got to be discarded.

Following three doses of OPV, seroconversion rates average 65, 96%, and 63% for types 1, 2 and 3, respectively.

Undoubtedly, multiple doses of OPV are required before 90–95% of children develop immune responses to all three poliovirus types.

Though immunogenicity of OPV is excellent in developed countries, in the low income countries around the tropical and subtropical belt, it is poor. Such a variation in immunogenicity is not a feature of eIPV.

Depending on the strain(s), OPV may be trivalent, bivalent, and monovalent (Box 2.1).

Inactivated Polio Vaccine (IPV)/Enhanced Inactivated Polio Vaccine (eIPV)

The IPV (more rationally, eIPV), is an enhanced formaldehyde killed poliovirus, grown in monkey kidney cell/human diploid cells and administered parenterally.

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Box 2.1: Features of three types of OPV

Trivalent OPV: A trivalent vaccine (tOPV) consists of a suspension of attenuated poliovirus types 1 (Brunhide), 2 (Lansing) and 3 (Leon). Since it was expected to provide protection against all the three polio strains, it dominated the scene all through until recently.

Monovalent OPV: mOPV is presumably 2.5–3 times more efficacious than tOPV since competition between different polio viruses is eliminated. Since 2005, mOPV containing type 1 or type 3 virus is being employed in India for pulse immunization. It was only in 2010 that the bivalent OPV (bOPV) containing type 1 and type 3 virus, was introduced for pulse immunization.

Bivalent OPV: Though polio type II got eradicated years ago, two remaining strains (PV1 and PV3) proved stubborn. PV1 is a more severe strain of the virus, while PV3 is more common and spreads rapidly. In January 2010, the Government of India launched a completely new bivalent oral polio vaccine (bOPV), after its fast-track development to attack PV1 and PV3 strains in the hope that it would work better than the trivalent (attacks all three strains) and monovalent vaccines (attacks single strain). Mercifully, the strategy worked, paying dividends.

The bOPV, first developed and tested in India, proved to be very effective. The impact of this new tool has been impressive against both remaining polio virus types 1 and 3, according to the National Polio Surveillance Project (NPSP) of the WHO. Not a single new case of the deadly PV1 (in fact, any of the three types) has been encountered over the past one year. The bOPV has provided protection levels against both virus types that are similar to those achieved by each of the respective monovalent oral polio vaccines.

This is a highly immunogenic vaccine. However, its immunogenicity is vulnerable to be dampened by the presence of maternal antibody in the very young infant, especially up to the age of 8 weeks.

The eIPV can be administered along with all other childhood vaccines and can be used in combination with DTwP/DTaP, Hib, and hepatitis B vaccines without compromising seroconversion or increasing AEFI.

Notably, the eIPV is a very safe vaccine. Several countries, especially the prosperous ones, have shifted from all OPV to sequential OPV-e IPV schedules and all eIPV schedules with elimination of wild polio (Box 2.2).

In India, the eIPV is supposed to become indispensable in the post-eradication era when OPV shall need total withdrawal, perhaps in phases. Since vaccination against polio cannot be withdrawn, the only choice shall be eIPV.

OPV and Vaccine-associated Polio Paralysis (VAPP)[5,6]

According to World Health Organization (WHO), VAPP denotes "those cases of AFP which have residual weakness 60 days after the onset of paralysis and from whose stool samples, vaccine-related poliovirus but no wild polio virus is isolated." VAPP may occur in the vaccine recipient (recipient VAPP, occurring within 4–40 days of receiving OPV) or contact of the vaccine recipient (contact VAPP).

The risk of VAPP is higher with the first dose that "takes", with P2 virus and in patients with B cell immunodeficiency.

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Box 2.2: Polio vaccines: Fact sheet[2-4]

Oral Polio Vaccine (OPV)
Sabin strain type, live-attenuated vaccine that also induces humoral immunity, providing per dose efficacy of 30% worldwide and 10–15% in India. A highly heat-sensitive vaccine, having shelf-life of 6 months at 2–8°C. At –20°C, shelf-life zooms to 2 years. It is just 1–3 days at room temperature.

Brand name: OPV(Aventis Pasteur), Oral Polio Vaccine Monovalent (Panacea Biotec), Oral Polio Vaccine Trivalent (Panacea Biotec), Polio Vaccine Oral (Haffkine), Polio virus type 2 (PV2)

Indication: Protection against poliomyelitis.

Dose: 2–3 drops directly into child's mouth at birth (zero dose), then at 6 weeks, 10 weeks, and 14 weeks. Following these 4 primary doses, booster doses are administered at 15–18 months and 5th year. Thus, a total 6 doses are recommended. Pulse polio doses are in addition to these basic doses.

AEFI: Practically no side effects are seen; very rarely vaccine-acquired polio paralysis (VAPP)

Contraindications: Severe vomiting and diarrhea; immunodeficiency.

Storage: Vaccine carrier for transport to outreach center: 2–8°C.

Clinical level: Freezer (–5 to –15°C).

State and district levels: –20°C.

Inactivated Polio Vaccine (IPV)/ Enhanced Inactivated Polio Vaccine (eIPV)
Salk strain type, killed (inactivated) vaccine with 95–100% protective efficacy

Brand name: (Imovax polio)

Indications: Now that global eradication of polio is round the corner, over and above the OPV, the enhanced IPV has been introduced in the IAP immunization schedule. In addition to routine immunization against polio, it is especially indicated in immunocompromised children and for boosting the eradication endeavors.

Available as: Isolated polio vaccine and in combination with other vaccines.

Dosage: 0.5 mL (SC, IM) at 6, 10 and 14 weeks followed by a booster at 15–18 months. This is over and above the routine OPV.

AEFI: No significant side effects recorded so far.

Contraindication: Severe hypersensitivity.

Storage: 2–8°C.

The VAPP, a rare AEFI of OPV (incidence: 4 in 1 million doses in developing and 1 in 2.4 million doses in developed countries), occurs due to loss of attenuating mutations and reversion to neurovirulence during replication of the vaccine virus in the gut.

In India. According to estimates, 181 cases of VAPP occurred in 1999.

OPV and Vaccine-derived Polio Virus (VDPV)

Since we have a massive OPV campaign for many years, emergence of VDPV is expected. During 2000–2009, as many as 13 outbreaks of cVDPVs were

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reported from 13 countries in 3 continents, with over 421 cases, including a large outbreak in Nigeria caused by cVDPV type-2.

In each of these incidents, immunity gaps were identified as potential risk factors, and OPV was used to control the outbreak. A total number of 24 VDPV was reported between April 2009 and January 2010 in India.

Polio Vaccines and Herd Immunity

This herd effect of OPV (phenomenon of immunized individuals affecting the epidemiology of infection and consequently disease in the unimmunized segment of population) seen in the industrialized countries is not visible in India. The following points favor this observation:

1. Repeated doses of OPV have to be given to the same group of children, with virtually 100% coverage, before wild virus transmission could be stopped.
2. The median age of polio in India has not shifted to the right and remained stationary at 12–18 months from prior to introducing immunization till now. On the contrary, IPV with its high immunogenicity and efficacy, induces high levels of antibodies which spill over to the gut and thus prevent transmission potential of immunized individuals besides protecting them.

Thus, contrary to the conventional teaching, IPV exhibits a demonstrable herd effect.

POLIO VACCINES: INDIAN PERSPECTIVES

IAP Advisory Committee on Vaccines and Immunization Practices (ACVIP)[1] recommends birth dose of OPV, 3 primary doses of IPV at 6, 10 and 14 weeks, 2 doses of OPV at 6 and 9 months, another dose of IPV at 15–18 months and OPV at 5 years.

According to the IAP-ACVIP, in situations where IPV is not affordable or is unavailable, the primary series must be completed with 3 doses of OPV at 6, 10 and 14 weeks. Furthermore, all OPV doses (mono-, bi- or trivalent) offered as a part of supplementary immunization activities (SIAs) should also be given.

In the opinion of IAP - ACVIP, the risks of leaving large population without any protection against future polio outbreaks being grave, the only safe option is to introduce IPV and achieve high coverage before discontinuing OPV. IAP-ACVIP believes there is a need to chalk out a clear strategy on how to deal with the issues like OPV cessation plans, global synchronization versus regional/national synchronization, duration of AFP surveillance, tackling of future outbreaks of both wild and vaccine viruses, role of IPV in controlling future outbreaks of cVDPVs, development of safe and affordable IPV, etc. IAPCOI thinks that there is a need to develop country-specific economic models for employing universal IPV during post-eradication era.

Box 2.3 gives IAP-ACVIP[1] recommendations on poliovirus vaccines.

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Box 2.3: IAP-ACVIP recommendations poliovirus vaccines

Routine vaccination

- *Recommended schedule*: Birth dose (0 dose) of OPV, 3 primary doses of IPV at 6, 10 and 14 weeks, followed by two doses of OPV at 6 and 9 months
- Birth dose of OPV usually does not lead toVPP
- OPV in place of IPV, if latter is unfeasible, minimum 3 doses
- Additional dose of OPV on all SIAs
- *IPV*: Minimal age 6 weeks
- *IPV*: 2 instead of 3 doses can also be used if primary series started at 8 weeks and the interval between the doses is kept 8 weeks
- No child should leave the immunization facility without polio immunization (IPV or OPV) if indicated by schedule.

Catch-up vaccination

IPV catch-up schedule: 2 doses at 2 months apart followed by a booster after 6 months of previous dose.

BIDDING GOODBYE TO POLIO: SUCCESS STORY[7,8]

The availability of two effective vaccines against poliomyelitis for the past five decades has ensured remarkable decline in the global burden of disease. They were developed in the USA during 1950s, first the inactivated polio vaccine (IPV) by Jonas Salk and later the live oral polio vaccine (OPV) by Albert Sabin. The Global Polio Eradication initiative was launched in 1988 using oral polio vaccine (OPV) as the eradication tool and employing a four pronged strategy comprising high routine immunization coverage, supplementary immunization activities (SIAs)/pulse immunization, AFP surveillance, and "Mop- up" immunization. The initiative was hugely successful with reduction of polio cases from 350,000 in 1988 to less than a 1000 cases in 2010.

Only four countries Pakistan, Afghanistan, India, and Nigeria ("PAIN" remained endemic till recently. Now India has eased out of this PAIN.

Wild virus type 2 has not been isolated since 1999.

In 2005, new monovalent polio vaccines (mOPV type 1 and type 3) were licensed and used to enhance the impact of supplementary immunization activities (SIAs) in the key remaining reservoirs of wild polio. Despite the use of mOPVs and the intensification of the global eradication efforts in 2007, indigenous wild poliovirus type 1 (WPV1) and 3 (WPV3) transmission continued in geographically limited areas of four countries: Nigeria, India, Pakistan, and Afghanistan. The challenge of interrupting the residual WPV transmission in these areas has been compounded by the recurrent exportation of WPV from northern Nigeria and northern India into previously polio-free areas within and outside their borders.

While mOPVs have provided the GPEI with much more potent tools for rapidly building population immunity, optimizing the balance of mOPVs has proven much more difficult than originally anticipated, leading to alternating outbreaks of type 1 and 3 poliovirus in certain settings and prompting the fast-track development of a completely new 'bivalent' OPV (bOPV).

Following intelligent use of mOPVs and bOPV, the total number of wild polio cases was reduced to 41 in year 2010 in India.

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Box 2.4: Historical landmarks in the polio elimination from India

- 1988: Launching of the Global Polio Eradication Initiative (GPEI) with the sole objective of eradicating transmission of WPVs from the globe by the year 2000
- 1990: Launching of the India Polio Eradication Initiative (IPEI) monitored by Government of India with an advisory body (India Expert Advisory Group) and implemented by National Polio Surveillance Project (NPSP) in collaboration with Union and State Governments
- 2000: All countries, except Pakistan, Afghanistan, India, Nigeria ("PAIN"), Egypt and Niger achieved the WHO's goal of eradcating polio. Later, Niger and Egypt too attained the goal
- 2009: India has more polio cases than any other country in the world, recording 741 cases of polio—nearly half the number of global cases
- 2010: Transmission of WPV-3 and 1 interrupted in India—a great leap towards polio eradication from India
- 2011: Only one case of WPV3, from Kolkata, West Bengal on January 13, 2011 and nil case from the high polio endemic "hotspots" of UP and Bihar, for the first time in the history since GPEI was launched. This remarkable achievement was due to the use of bOPV 1 and 3 in campaign during National and Sub-National Immunization Days in the high Polio endemic 'hot spots' of UP and Bihar
- However, a disturbing observation was that 7 cases of cVDPV from 6 states were a matter of concern since the definition of true Polio Eradication is NIL transmission of NOT ONLY Wild Polio Virus BUT ALSO NIL cases due to Vaccine Derived Polio Virus (VDPV) as well. Five out of 7 cases were due to circulating P2 Vaccine derived virus and 2 cases due to ci P3 VDPVs
- 2012: No polio case detected throughout the country since January 13, 2011. India declared polio-free though a minimum of 3 years of continuing polio-free state in the country will qualify it for eradication of polio
- 2015: Polio is eradicated from India.

POLIO ERADICATION IN INDIA: HISTORICAL LANDMARKS

Some historical landmarks in the polio eradication in India are highlighted in Box 2.4.[8-10]

FUTURE APPROACH AND PERSPECTIVES

India's ambitious journey towards elimination of polio, though at times bumpy, has finally come close to realization.[10] If all goes well, in 2014, India should be joining the fraternity of countries where from polio stands eradicated. There is, however, an important rider: Let us remain vigilant. We have been polio-free only since January 2011. We have another nearly 2 years to go before we could be declared having eradicated polio. Clinical and virological surveillance must not be relaxed at any cost during this period and perhaps for some years that shall be ahead of 2014.[10] Even emergence of a single child with fresh polio can spoil the broth.

What should be the policy towards OPV and IPV ? Logically, by 2014, we should be withdrawing OPV and introducing IPV. Else, the threat of VDPV and VAPP shall continue to haunt us.

All said and done, as an essential prerequisite for withdrawing OPV, the Government of India must assure introduction of IPV in order to establish high immunity prevalence.

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SUMMARY AND CONCLUSION

Poliomyelitis is an acute viral infection (RNA enterovirus) characterized by clinical manifestations varying from nil to rapid paralysis. Type 1 strain (Burnhide) causes large epidemics, type 2 (Lansing) isolated cases and small outbreaks and type 3 (Leon) small epidemics. Asymptomatic (silent, inapparent), abortive, nonparalytic and paralytic (spinal, bulbar, bulbospinal or encephaltic) forms are known. Until recently, it was the most common cause of physical disability and handicap in the low-income countries.

Two types of polio vaccines are available: oral polio vaccine (OPV) which may further be trivalent, bivalent, or monovalent and IPV. Contrary to the earlier understanding, it is the IPV that has a better herd effect. Rarely, OPV may cause vaccine-related paralysis.

Consequent upon the Global Polio Eradication Initiative, employing polio vaccine as a part of basic immunization plus pulse polio campaign, effective surveillance system and mopping up by door-to-door immunization, the disease is close to elimination/eradication. Now that India has been polio-free over more than 3 years, WHO has made a declaration that polio stands eradicated from India.

Now, we are already in the thick of shift from all OPV to sequential OPV-IPV schedules. In the next few years, it shall be "all IPV" schedules as has been the case with the Western countries.

KEY LEARNING POINTS

- Poliomyelitis, an acute viral infection (RNA enterovirus) characterized by clinical manifestations varying from nil to rapid paralysis, has been the most common cause of physical disability and handicap in the low-income countries.
- Two types of polio vaccines are available: oral polio vaccine (OPV) which may further be trivalent, bivalent, or monovalent and IPV.
- Contrary to the earlier understanding, it is the IPV that has a better herd effect. Rarely, OPV may cause vaccine-related paralysis.
- Consequent upon the Global Polio Eradication Initiative, employing polio vaccine as a part of basic immunization plus pulse polio campaign, effective surveillance system and mopping up by door-to-door immunization, the disease is close to elimination/eradication.
- At least two more years are required to complete a minimal of 3 years (Nov. 2010–Nov. 2013) of polio-free India for enabling WHO to declare that polio stands eradicated from India.
- Now that we are close to elimination/eradication of polio from India, time has come for shift from all OPV to sequential OPV-IPV schedules.
- Once elimination/eradication becomes a reality, it shall be "all IPV" schedules as has been the case with the Western world.

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CONCERNS, CONFUSIONS AND CLARIFICATIONS: INTERACTIVE REVIEW

How is OPV produced?

OPV is grown in monkey kidney cell cultures. Then, it is stabilized with magnesium chloride. It is presented in a buffered salt solution, with light pink color indicating the right pH.

How does OPV work after it is swallowed?

To begin with, the vaccine virus reaches the intestines. Here, it tends to establish a kind of subclinical infection ("take"). This is followed by development of an immune response occurs. This immune response forms the basis of future protection against the crippling viral disease.

Is it safe to give OPV along with booster dose of triple (DPT/DTP) vaccine?

Yes, it is safe and problem-free.

Is it safe to give OPV along with a dose of vitamin A?

Undoubtedly, it is safe. Millions of doses of the two have been given almost simultaneously without any problem.

What is the cut-off age for giving OPV?

Till 5 years of age.

Why is it that, in spite of such an extensive use, OPV has not succeeded in eradicating polio so far?

Quite a good query. Until recently, OPV was believed to mimic natural infection, spread widely in the community and immunize children in community (contact immunization), and produce excellent mucosal immunity to protect not only from disease but also from subsequent infection. Due to these attributes, it was believed that it would eliminate transmission of wild polio virus when 3 dose tOPV coverage reaches 80–85% (herd effect). Unfortunately, that has not happened. Hence, now there has occurred a complete somersault in the concept. The current belief is that it is IPV that has a much better herd effect than OPV.

Is OPV better than IPV now that India is polio-free? or, else, is it other way round?

Once polio is eliminated from a country, ideally it should shift to "all IPV" as was done by affluent countries. This line of action may be beyond the reach of source-limited countries. The second best is sequential OPV-IPV schedules towards and soon after the elimination phase of polio. Later, only IP scheduled should be pursued. However, it is vital to maintain a very high coverage. This is the policy adopted by the Indian Academy of Pediatrics.

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Over very many years, we have been hearing that elimination of polio is around the corner. Will this ever happen globally?

Fighting polio was indeed a war rather than a sheer fight. Fortunately, a time has arrived when we can see its elimination/eradication very close now. With not a solitary case of polio seen in India ever since 13 January 2011, only three countries are left with some polio cases, namely Pakistan, Afghanistan, and Nigeria. Once these countries become polio-free in the next couple of years or so, stage shall be set for declaration of good bye to this wretched illness that left millions disabled in the past.

Parents often ask "Why does the child need to be given polio vaccine if the disease has been eliminated from India?" How should a practitioner handle this query?

Polio is close to eradication, not yet eradicated globally. It is only safe to stop vaccinations for a particular disease when that disease has been eradicated worldwide, as in the case of smallpox.

Does breastfeeding soon after OPV dose interfere with its "take" ?

No, it does not in a substantial way. Contrary to old practice, now there is no objection to breastfeeding immediately after OPV.

What are vaccine-derived polio viruses (VDPV)?

VDPV arise due to mutation and recombination in the human gut and are somewhat divergent from the parent vaccine virus. In addition to being neurovirulent, these are transmissible and capable of causing outbreaks. They have been classified into three groups:

1. Circulating VDPV (cVDPV) VDPV with evidence of virus circulation in the population causing two or more paralytic cases.
2. iVDPV- VDPV in the immunodeficient person, and
3. VDPV of ambiguous origin (aVDPV)—VDPV isolated from environmental sources or evidence of circulation not established.

During 2000–2009, 13 outbreaks of cVDPVs were reported from 13 countires in 3 continents, with over 421 cases. There was a large outbreak in Nigeria caused by cVDPV type 2.

In each of these incidents, immunity gaps were identified as potential risk factors, and OPV was used to control the outbreak.

What is the clinical significance of VDPVs?

These outbreaks of polio caused by these emerging viruses demonstrate the importance of achieving and maintaining high polio immunization rates. Risk factors for outbreaks due to cVDPV include dropping immunization coverage (both routine and SIAs), high population densities, tropical conditions, and previous eradication of wild virus.

With polio eradication being in sight, what is the justification for giving both OPV and IPV to children?

The IAP has put forward the following reasons for giving both the vaccines in India until IPV completely takes over from OPV which shall then be withdrawn, or until better guidelines are provided by the WHO or its agencies:

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- Excellent and highly predictable immunogenicity, efficacy, and safety of IPV
- OPV use should be continued at present in concordance with the government policy
- Better mucosal immunity of OPV and IPV combination schedule as compared to IPV alone
- The risk of VAPP with this combined OPV and IPV schedule is extremely low as the child receives OPV at the time when he/she is protected against VAPP by maternal antibodies. Subsequently he/she is protected from VAPP by IPV. Even if we adopt an all IPV schedule, the child may still be at a small risk for VAPP through exposure to the oral polio vaccine virus through contacts/ environment before he/she receives his/her first dose of IPV
- OPV and IPV used simultaneously in combination in the trials in Gambia, Oman, Thailand, and Pakistan have shown higher levels of seropositivity as compared to all OPV or IPV alone schedules. In the Gaza strip combined IPV-OPV use reduced the incidence of paralytic polio from 10 to less than 2 cases per 100,000 persons in the first 3 years, and it further reduced to 0.16 per 100,000 cases in the next 5 years
- Furthermore, the concurrent use of OPV may compensate for somewhat inferior seroresponse (particularly against types 1 and 2 serotypes) of IPV when used in accelerated 6, 10, and 14 week schedule.

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