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REVIEW ARTICLE

Global Polio Eradication Initiative (GPEI): Future Perspectives and Need for a New Generation of Inactivated Poliovirus Vaccine

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Abstract:
More than two decade-old Global Polio Eradication Initiative (GPEI) has finally tasted success and wild poliovirus is now on the verge of eradication. The pre-eradication era was full of challenges and a great learning experience for all those involved with this tedious process. Many new phenomena emerged and new information about poliovirus learned during this campaign. Many new developments such as vaccine-derived polioviruses (VDPVs) were not anticipated and resulted in serious thinking regarding post-eradication vaccine policy. As a result, the post-eradication era is going to be even more complex, more uncertain and complicated than the pre-eradication era. There are many issues that warrant urgent attention not only by the perpetrators of GPEI but by the individual member country. There is almost unanimity that continuous post-eradication use of oral polio vaccine (OPV) is incompatible with the eradication, hence, OPV will need to be discontinued. However, there is utter confusion on the face of future polio immunization after eradication. Few of the most contentious issues of immediate post-eradication era are how to safely stop and withdraw OPV usage world-wide and whether universal inactivated poliovirus vaccine (IPV) be used or not, especially in developing countries. Although both OPV and IPV have proven highly effective in the past, neither the live nor the current IPV are optimal for use in the post-eradication setting. Therefore, rigorous efforts are urgently needed to develop a new generation of inactivated vaccine that is risk-free and affordable and can be produced even in developing country setup. This review provides an insight to the all the issues related to post-eradication era and also discusses briefly the need of having a third generation IPV.

Keywords: *Polio eradication, post-eradication era, inactivated poliovirus vaccine*
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Introduction

Since its inception in 1988, the Global Polio Eradication Initiative (GPEI) is marred with frequent delays, unprecedented threats and challenges and frequent change of its strategy to achieve the final goal. Many stalwarts of eradication initiative have also started challenging the prudence behind continuation of expensive, labor intensive initiative in resource poor countries at the cost of some of the more pressing health issues [1-3]. The GPEI has undergone significant evolution in response to these challenges over the course of its lifetime. Though the GPEI is slowly but surely moving toward its culmination, however, to achieve total success, it needs to tread extremely cautiously especially in some of the traditionally endemic countries [4].

The greatest challenges in front of GPEI right now

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are: first, to achieve interruption of wild polio transmission in the remaining four endemic countries at the earliest along with halting the reintroduction of the disease to polio-free countries through importation; second, devise strategy to safely discontinue use of OPV in a synchronized coordinated way all over the globe and decide on future vaccination policy including the switch to universal use of inactivated poliovirus vaccine (IPV) [5].

Post-eradication issues:

There are many issues to deal with after achieving the zero polio status. They include: how will OPV be stopped? Simultaneous globally synchronized or nationally synchronized way? Should IPV be used universally after OPV cessation? When should IPV be started? [6]. The current plan of action of GPEI is to discontinue OPV globally, after eradication is certified by the Global Commission for the Certification (GCC) of the Eradication of Poliomyelitis, but without any provision for IPV [7]. It is evident that developed countries are already using or will soon switch to IPV, principally to avoid sporadic or epidemic vaccine-associated paralytic poliomyelitis (VAPP) associated with OPV. Some of the more affluent developing countries will also avail themselves of IPV [8]. Developing countries may also be loath to risk resurgence of polio if OPV immunization is stopped, as a result of uncertainties concerning persistent circulation of wild or revertant vaccine viruses in normal and immuno-suppressed individuals [9,10]. Amongst all these issues described above, the most complex and complicated would be how to stop and withdraw OPV usage world-wide. It is desirable to stop OPV simultaneously in all countries [6].

Cessation of OPV use was always a part of the polio eradication campaign scenario, based on cost-saving expectations as well as prevention of VAPP. The existence of vaccine-derived polioviruses (VDPVs), their ability to produce outbreaks, and the demonstration that they exhibit pathogenicity similar to wild type strains significantly changed the risk-benefit analysis associated with the 'endgame' of the polio eradication campaign [11]. This coincided with a global shift in public perception of international security risks that was provoked by the events of September, 2001. It became obvious that the emergence of large populations of unvaccinated individuals following OPV cessation could risk re-starting a global polio pandemic caused by either VDPV, wild-type polioviruses, or chemically synthesized virus [12], re-introduced into circulation either accidentally or intentionally [13,14]. The actual risk of re-starting polio circulation is not known, but limited experimental data suggest it could be quite serious [15].

WHO stand on post-eradication vaccination policy:

According to WHO, after interruption of wild poliovirus, continued use of OPV would compromise the goal of a polio-free world (Expert consultation on vaccine-derived polioviruses. September 2003, Geneva). In 2006, they reaffirmed their stand by stating "continuing OPV after poliovirus transmission interruption globally is not compatible with eradication as it could lead to the re-emergence of poliomyelitis globally" (16). The stated strategy of WHO is to stop using OPV in a single day, once eradication has been presumed to occur [16]. This strategy involves simply observing for poliovirus circulation and for cases poliovirus-induced paralysis in the absence of vaccination.

Some are skeptical of this strategy because of the risk of continued asymptomatic infections by wild or vaccine-derived polioviruses; malicious introduction of virulent polioviruses, an event that has already occurred in India; [17] or inadvertent escape of virulent virus from laboratories [18,19].

In order to pursue a safe long-term strategy, we must maintain a high level of immunity against poliovirus. Deliberate creation of an immunologically naïve population is neither medically nor ethically acceptable. Considering the problems of OPV, the only realistic way to maintain worldwide immunity against poliomyelitis is to replace OPV with IPV, administered as part of a universal routine immunization program [20].

Virtues and Shortcomings of current IPV formulation:

IPV is highly effective in producing immunity to poliovirus and protection from paralytic poliomyelitis. The original Salk vaccine had been 60 - 70% effective against PV1 (poliovirus type 1), over 90% effective against PV2 and PV3, and 94% effective against the development of bulbar polio [8].

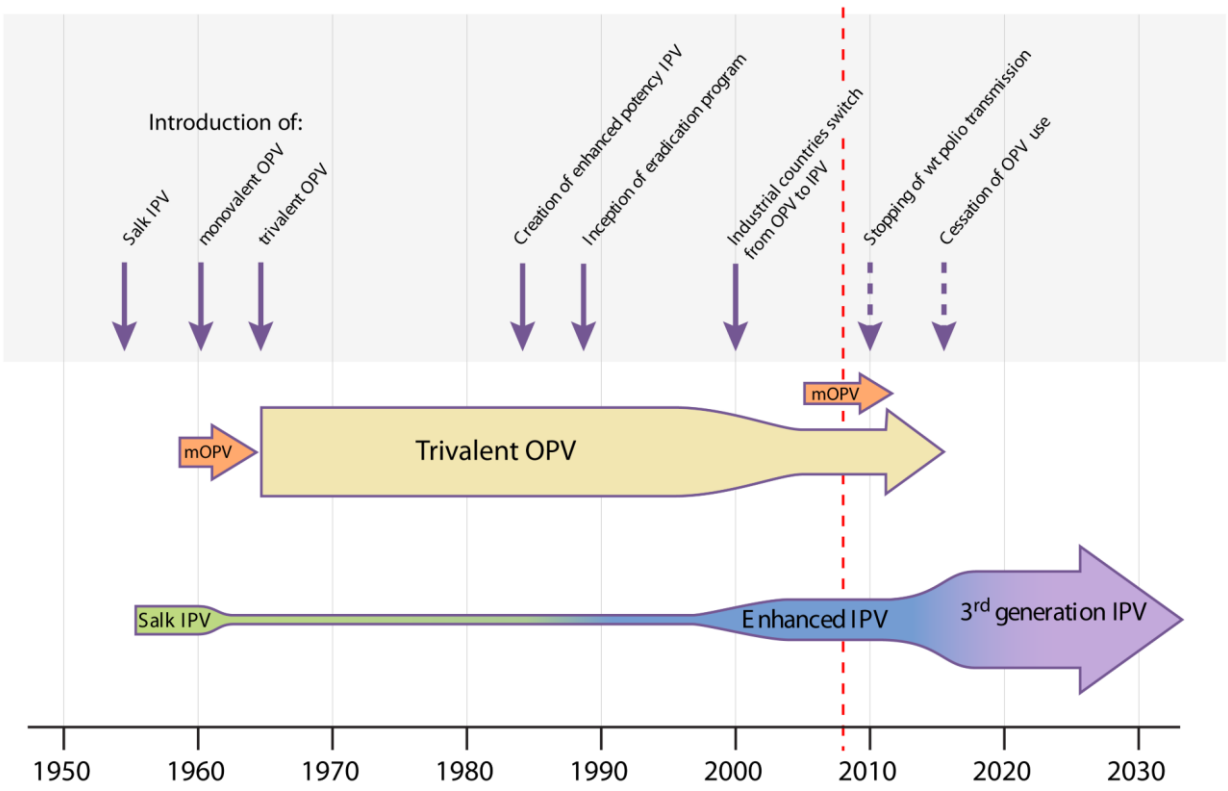

Figure 1. Past and projected global poliovirus vaccine usage.

(Vertical arrows indicate the years of major changes in vaccine product utilization. Dotted vertical arrows denote estimates of future years of possible changes to come. Horizontal arrowsindicate the use of the different IPV and OPV products. The thickness of the horizontal arrows (not to scale) suggests the amount of vaccine utilized during the indicated time period). (From Chumakov K, Ehrenfeld E. New generation of inactivated poliovirus vaccines for universal immunization after eradication of poliomyelitis. Clin Infect Dis. 2008; 47:1587-92.)

However, with the current enhanced-potency (eIPV), 90% or more of vaccine recipients develop protective antibody to all three poliovirus types after two doses, and at least 99% are immune following three doses [8]. However, among the shortcomings of current IPV, are comparatively lower gut immunity than OPV, need of injection to administer the dose, high production cost, shortage of vaccine supply, and need of wild polioviruses as substrate to produce it [8]. Though IPV appears to produce less local IgA in gastro-intestinal tract than does OPV; however, IPV produces almost comparable local immunity in the pharynx .The duration of immunity with IPV is not known with certainty, although it probably provides protection for many years after a complete series [8,21]. IPV is the polio vaccine of choice for immuno-suppressed individuals and in most circumstances is the vaccine of choice for adults. Since the 1960s, the controversy that has consumed much ink is the choice of IPV or OPV for routine vaccination in infancy [8]. In essence, the arguments for IPV are safety, predictable immunogenicity, and the possibility of its inclusion in combination vaccines [8]. While OPV dominated the world poliovirus vaccine usage for many decades, unarguably, the future era belongs to IPV and its new avatar (Figure 1).

Arguments against widespread use of IPV in developing countries:

The principal arguments offered against conversion from OPV to IPV in developing countries are cost, shortage of vaccine supply and decreased intestinal immunity [7]. To some extent the first two problems are related because large production volumes reduce costs of quality control and allow better planning. So far, companies have not been urged to produce more IPV. However, the more logical response to cost is

that IPV should not be used as a monovalent vaccine with the attendant expenses of separate administration, but rather as part of a combination vaccine [22]. Combinations containing IPV based on diphtheria-tetanus-pertussis vaccines are available. If there were a demand, and bearing in mind the oft-stated desire to bring new vaccines to the EPI schedule, the cost of IPV would be negligible as part of acellular or whole cell DTP-based combinations. Whereas the cost of vaccine purchase would be increased, the cost of vaccination would be reduced by the elimination of national vaccine campaigns and by a less exigent cold chain [8].

Vaccine supply is definitely a problem, as there are currently only two major manufacturers of IPV, and their joint capacity would not permit vaccination of every child in the world. If all industrialized countries were to use IPV, about 40 million doses would be needed, which is about half of current production capacity, leaving insufficient vaccine for developing countries. Of course, this problem is somewhat circular in that the manufacturers have not received the call to increase their capacity. An annual production of between 200 and 300 million doses of IPV is feasible in the immediate future [6,8]. To reduce the need for a larger supply, the use of IPV in developing countries could be targeted to countries or regions of countries surrounding areas where poliovirus is supposedly eliminated, so that appearance of the virus could be recognized by isolation from excreta, rather than by outbreaks of paralysis.

If poor countries could acquire IPV more cheaply, this and other post-eradication weakest links would fall away. Suppose poor countries could protect their populations as cheaply using inactivated as live oral vaccine. Then they would have nothing to lose by stopping oral vaccination [23]. The likelihood of a post-eradication outbreak of vaccine-derived viruses would be unchanged, but the consequences of such an outbreak would be less dire, because countries could maintain population immunity at no additional cost (relative to continuing to oral vaccination), and without making other states more vulnerable [23].

However, there are substantial financial and logistical challenges to its implementation, as well as certain scientific issues that must be addressed before universal IPV use is deemed permanent and safe. Many experts are now convinced that mere switchover to IPV would not serve as a panacea to all post-eradication hitches and a future poliovirus vaccine would be needed during post-eradication era especially in resource-poor developing countries [24]. Even those who are currently running and in charge of GPEI, have publicly opined in favor of such a need [25,26].

New generation IPV:

IPV has demonstrated an excellent safety and efficacy record. Its relatively minor shortcomings such as poor induction of intestinal immunity and the need to administer by injection do not justify development of a new product. However, even though the current IPV could continue to be successfully used, other considerations support a proposal to develop a new generation IPV product [27]. Here lies a challenge to the research community: they should continue their efforts to improve IPV and produce a vaccine that combines the advantages of the two present day vaccines. This could be done by using novel adjuvants and routes of administration, or by exploring other innovative approaches [11].

A stable supply of inexpensive IPV for use in low and middle-income countries will likely require substantial increases in worldwide production capacity. Scaling up the existing manufacturing base may reduce the vaccine price, but maximum cost reduction would be achieved by building production facilities in developing countries. However, ensuring containment of wild-type polioviruses [27], from which the current IPV is made, in new production facilities that lack experience and that are situated in regions with inadequate population immunity raises major concerns. Thus, development of IPV from non-pathogenic strains becomes a top priority. Many such options are available such as use of Sabin virus to develop a new ‘Sabin IPV’, modification of the 5′ non-coding region of the viral genome to work as alternate substrate to manufacture IPV, altering polymerase fidelity and nucleotide sequences to display a different codon set, swapping different but synonymous codons within the same sequence, micro RNA sequence insertion, and use of novel adjuvants are the few ways that can be tried to develop a new generation of IPV for use during post-eradication era [27]. All these novel approaches have been tested in preliminary experiments and showed promising

results for developing non-pathogenic polioviruses with wild-type antigenicity. However, research is still needed to demonstrate that IPV made from such strains is feasible to produce and efficacious. It may be prudent to create strains that combine some of these approaches.

Need of the hour:

Recent events on the global scene make it timely not only to reassess the tactics of stopping wild-poliovirus circulation, but also to chart policies beyond eradication. The process of devising a new vaccine policy against polio for the post-eradication era should be started in all those countries that have not as yet considered this issue worth debating. A new policy and its implementation will take time since transition cannot be made overnight. The few recent publications from India have charted out roadmap for this transition [6,28]. According to one publication, India, a highly endemic developing country, it should incorporate IPV in its national vaccination schedule, achieve very high coverage and then only withdraw OPV [28]. This could be done simultaneously or through staggered transition throughout the nation – even if the rest of the world has not stopped OPV [28]. Similar exercises are also needed from other developing countries. As far as future IPV deployment is concerned, the issue of limited supply and cost can only be resolved if the developing countries are allowed to produce IPV locally. However, to curtail the risk of release of wild virus from the IPV production sites in developing countries, we need to make IPV from more safe substrates. Continued research on poliovirus should be encouraged and should focus on the improvement of the existing IPV and development of even new products. These improvements would include cost reduction, bundled delivery with other vaccines for children and boosting its ability to induce local immunity. The use of combination vaccines throughout the world could provide an added public health benefit, as it could increase the cost-efficiency of the programme and prevent countries from dangerously stopping polio immunization for financial motives [11]. In addition, the development of fundamentally new vaccines, as well as efficacious anti-polio drugs, should be explored. Such efforts could radically change vaccination policy decisions and eventually lead to the true eradication of poliomyelitis.

REFERENCES

1-Arita I, Nakane M, Fenner F. Public health. Is polio eradication realistic? Science 2006; 312: 852-854.

2- Roberts L. Global health. Polio eradication: is it time to give up? Science 2006; 312: 832-835.

3- Phadke A, Kale A. The mirage of polio eradication. Natl Med J India. 2004; 17: 282.

4-Vashishtha VM. Polio eradication in India: need for caution. Indian J Pediatr. 2009; 76:757.

5-World Health Organization. Global Polio Eradication Initiative Strategic Plan 2004-2008. Weekly Epidemiol Rec 2004; 79: 55-57.

6- Vashishtha VM. Round Table Conference Series, Number 24. Polio Eradication: Challenges and opportunities. Proceedings of 24th Round Table Conference on Polio Eradication, Ranbaxy Science Foundation, New Delhi, 2010 , pp 67-82.

7-World Health Organization. Introduction of inactivated poliovirus vaccine in to oral poliovirus vaccine-using countries. Wkly Epidemiol Rec 2003; 78:241-250

8- Plotkin SA, Vidor E. Poliovirus vaccine-inactivated. In Vaccines Ed. Plotkin SA, Orenstein W, Offit P. Sauders, 5th Edition, 2008, pp 605-629.

9- Schoub BD: The risks of stopping vaccination: perspectives from the developing world. Bull World Health Organ 2000; 78:360-361.

10-Fine PE: Gaps in our knowledge about transmission of vaccine-derived polioviruses. Bull World Health Organ 2000; 78:358-359.

11-Chumakov K., Ehrenfeld E., Wimmer E. and Agol VI. Vaccination against polio should not be stopped. Nature Reviews 2007; 5: 952-958.

12-Cello, J.; Paul, AV.; Wimmer, E. Science. 297. New York, NY: 2002 Aug 9. Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template; p. 1016-8.

13-Agol VI, Chumakov K, Ehrenfeld E, Wimmer E. Don't drop current vaccine until we have new ones. Nature 2005 16;435:881.

14-Bompart F. Vaccination strategies for the last stages of global polio eradication. Indian pediatrics 2005 ;42:163–9.

15-Retrospective analysis of a local cessation of vaccination against poliomyelitis: a possible scenario for the future. Journal of virology 2003;77:12460–5.

16- Aylward RB, Sutter RW, Heymann DL: Policy. OPV cessation–the final step to a 'polio-free' world. Science 2005; 310:625-626.

17-Deshpande JM, Nadkarni SS, Siddiqui ZA: Detection of MEF-1 laboratory reference strain of poliovirus type 2 in children with poliomyelitis in India in 2002 & 2003. Indian J Med Res 2003; 118:217-223.

18-Diamond B: Global polio campaign doomed to fail, experts warn. Nat Med 2005; 11:1260.

19- Agol VI, Chumakov K, Ehrenfeld E, Wimmer E: Don't drop current vaccine until we have new ones. Nature 2005; 435:881.

20-Arita I, Nakane M. Road map for polio eradication--establishing the link with millennium

development goal no. 4 for child survival. Japanese journal of infectious diseases 2008;61:169–74.

21-Atkinson W, Hamborsky J, McIntyre L, Wolfe S (eds.). Poliomyelitis. Epidemiology and Prevention of Vaccine-Preventable Diseases (The Pink Book) 2007; 10th ed.. Washington DC: Public Health Foundation. pp.101–14.

22-Kimman TY, Book N: The polio eradication effort has been a great success—let's finish it and replace it with something even better. Lancet Infect Dis 2006; 6(10):675-678.

23-Barrett S. Polio Eradication: Strengthening the Weakest Links. Health Affairs 2009; 28: 1079–1090.

24-Arya SC, Agarwal N. Prospective inactivated or live poliovirus vaccine: effectiveness in the 21st Century. Expert Rev Vaccines. 2009 ;8:127-30.

25-Roberts L. Polio eradication. Looking for a little luck. Science. 2009; 6;323(5915):702-5.

26-Roberts L. Polio eradication. Rethinking the polio endgame. Science. 2009;6;323 (5915):705.

27-Chumakov K, Ehrenfeld E. New generation of inactivated poliovirus vaccines for universal immunization after eradication of poliomyelitis. Clin Infect Dis. 2008; 47:1587-92.

28- John TJ, Vashishtha VM. Eradication of vaccine polioviruses: why, when & how? Indian J Med Res 2009; 130: 491-494.