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Role of Inactivated Polio Vaccine in Endgame of Polio

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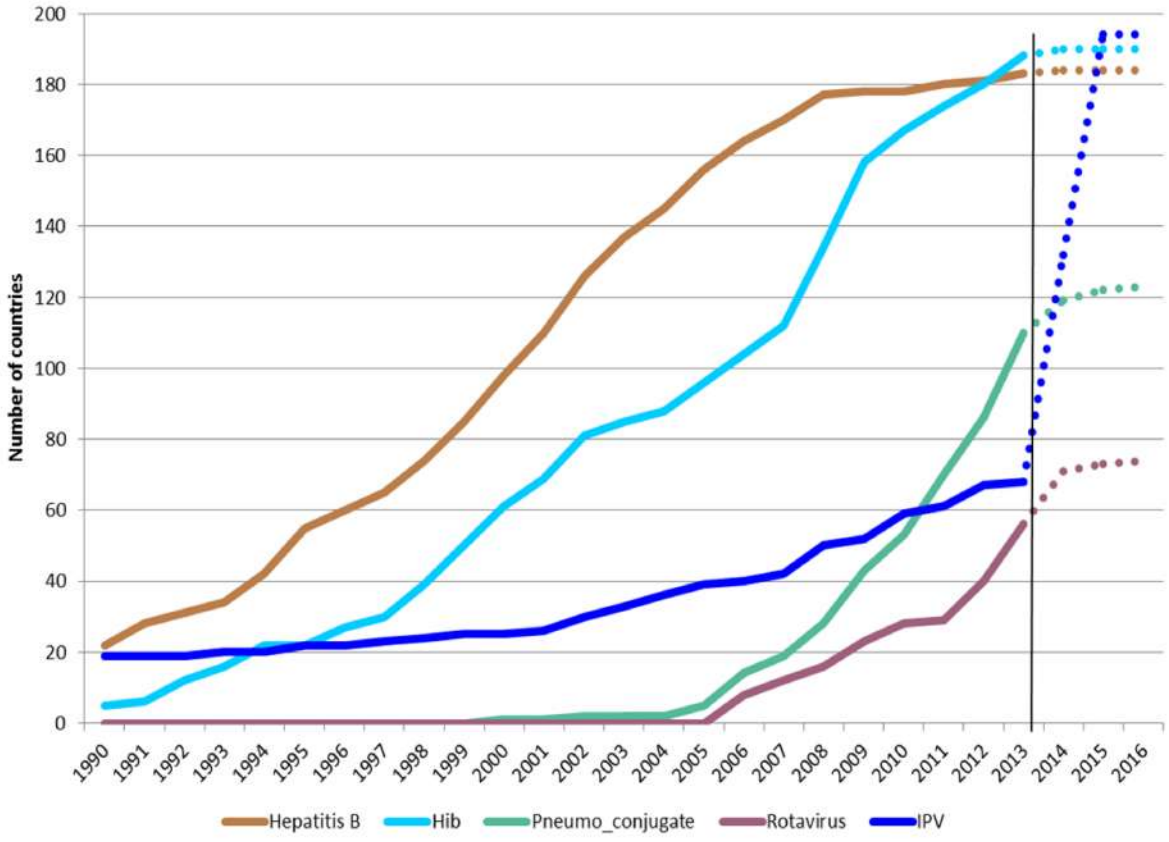
The poliovirus is now only endemic in three countries worldwide: Afghanistan, Nigeria and Pakistan, with outbreaks in the Horn of Africa, central Africa and the Middle East. With the global eradication effort being closer than ever to stopping this disease in its tracks, these steps towards the endgame have a major global significance. The recent launch in Nepal is a historic landmark in efforts to secure a lasting polio-free world, in particular in preparation for the phased removal of oral polio vaccines (OPVs) as outlined in the Global Polio Eradication Initiative (GPEI) Polio Eradication and Endgame Strategic Plan 2013-2018 (the Endgame Plan). Now that polio eradication is within reach and fewer cases of polio are reported, a new plan has been devised to minimise the risks of OPV while still achieving the global eradication goal. New evidence now clearly demonstrates that adding one dose of IPV to multiple doses of OPV at 14 weeks is the most effective method available to stop the virus and protect children, boosting immunity more effectively than just more doses of OPV. The recent launch in Nepal is a historic landmark in efforts to secure a lasting polio-free world, in particular in preparation for the phased removal of oral polio vaccines (OPVs) as outlined in the Global Polio Eradication Initiative (GPEI) Polio Eradication and Endgame Strategic Plan 2013-2018 (the Endgame Plan). India has already approved the plan and has started all out efforts to banish this vaccine preventable disease, other being small pox. The last case of small pox was eradicated in the Dadasiba block of district Kangra from Himachal Pradesh in 1976.

A recent paper published in *Journal of Virology* describes sporadic and sustained outbreaks of illness from circulating vaccine-derived polioviruses (cVDPV) in Nigeria[1] his study draws attention to what is often called the polio endgame–the vaccines and immunization activities that will be necessary to eradicate polio, given the ability of vaccine-derived viruses from the live polio virus vaccine to circulate and cause disease. To understand the complications of eradicating polio, it's necessary to know that three types of wild poliovirus have been identified. Types 1 and 3 are responsible for all cases of wild polio in the remaining polio-endemic countries of Pakistan and Nigeria. Type 2 virus is notorious for spreading VAPP. s Additionally, Type 2 vaccine virus is especially effective at spreading to secondary contacts and immunizing them. So, the vaccine's effectiveness for Type 2 is amplified in communities, and this may have hastened its disappearance. The milestone of eliminating wild Type 2 poliovirus, however, has been overshadowed by the fact that vaccine-*derived* Type 2 polioviruses (VDPV2) are emerging and causing vaccine-acquired paralytic poliomyelitis (VAPP) in some areas. This has been particularly common in Nigeria, but has also occurred in Madagascar, Afghanistan, Ethiopia, India, Democratic Republic of Congo, Somalia, and Yemen. (All cases involved VDPV2; Mozambique had an emergence of a Type 1 VDPV)[2]

In 2000, the island of Hispaniola which is home to Haiti and the Dominican Republic, was the first place where the existence of circulating vaccine derived poliovirus (cVDPV) was demonstrated[3]. As a live product, oral polio vaccine (OPV), once excreted, could enter the environment, re-assort with other enteroviruses, and produce cVDPV[4]. By 2008, the World Health Assembly was forced to concede that continued OPV vaccination was incompatible with polio eradication. OPV, and the accompanying risk of cVDPV, is incompatible with polio eradication. Polio eradication cannot be achieved while the use of OPV continues to cause rare cases of vaccine associated paralytic poliomyelitis (VAPP) and cVDPV. Some mechanism is required to prevent VAPP and cVDPV cases while still enjoying the operational and immunological advantages of OPV. This has led to a reconsideration of the potential solution through the careful application of combined

inactivated polio vaccine/oral polio vaccine (IPV/OPV) schedules as an interim step towards global cessation of OPV use[5].

In 2013, the World Health Assembly endorsed a plan that calls for the ultimate withdrawal of oral polio vaccines from all immunization programs globally. The withdrawal would begin in a phased manner with removal of the type 2 component of OPV in 2016 through a global switch from trivalent OPV to bivalent OPV (containing only types 1 and 3). To mitigate risks associated with immunity gaps after OPV type 2 withdrawal, the WHO Strategic Advisory Group of Experts has recommended that all 126 OPV-only using countries introduce, at least one dose of inactivated polio vaccine (IPV) into routine immunization programs by end-2015, before the trivalent OPV-bivalent OPV switch. The introduction of inactivated polio vaccine would reduce risks of reintroduction of type 2 poliovirus by providing some level of seroprotection, facilitating interruption of transmission if outbreaks occur, and accelerating eradication by boosting immunity to types 1 and 3 polioviruses[6].



WHA ask in 2012 for the Endgame Strategic Plan required IPV introductions in 126 countries globally within 20 months

With further restriction of the geographic extent of wild polio virus (WPV) circulation in the countries where polio is endemic, and provided that outbreaks after importation into polio-free countries can be prevented or interrupted promptly, interruption of global transmission could be achieved in the near future. The GPEI has developed the Polio Eradication and Endgame Strategic Plan for 2013–2018 to (1) interrupt all poliovirus transmission, (2) progressively withdraw OPV and introduce inactivated poliovirus vaccine, (3) certify polio eradication, and (4) transition assets and infrastructure to routine immunization programs as part of GPEI legacy [7]

The *Polio Eradication and Endgame Strategic Plan 2013-2018* was drawn up in response to the May 2012 World Health Assembly declaring the completion of poliovirus eradication to be a

programmatic emergency for global public health. Under this endgame plan to achieve and sustain a polio-free world, the use of oral polio vaccine (OPV) must eventually be stopped worldwide, starting with OPV that contains type 2 poliovirus (OPV type 2). At least one dose of inactivated polio vaccine (IPV) must be introduced as a risk mitigation measure. However, there are also challenges with using IPV, particularly in developing countries. IPV is administered as a shot, which is more complicated to give than the oral vaccine. Production capacity for IPV is limited as well, and vaccine manufacturers in emerging markets may need to begin producing the vaccine to ensure its global availability.

The steps involved are: (i) By end 2015, introduce at least 1 dose of IPV into all routine immunization systems, at least 6 months before the switch from trivalent oral polio vaccine (tOPV) to bivalent oral polio vaccine (bOPV, containing types 1 and 3 poliovirus).

(ii) During 2016, switch from tOPV to bOPV, which does not contain type 2 virus, in routine immunization and polio campaigns. (iii) Plan for the eventual withdrawal of all OPV. The tOPV to bOPV switch is necessary because: No wild poliovirus type 2 has been recorded over the past years and the risk of paralytic polio disease due to the type 2 component of OPV now outweighs its benefits. Since OPV is a live attenuated vaccine, in rare cases it can cause paralytic disease in two ways: as Vaccine Associated Paralytic Poliomyelitis or in outbreaks of circulating Vaccine-Derived Poliovirus. The vast majority of cVDPV outbreaks and a substantial proportion of the total VAPP cases are due to the type 2 components of OPV. Replacing tOPV with bOPV is key to ensuring the eradication of type 2 poliovirus. The switch from tOPV to bOPV will serve as a 'dry run' for the withdrawal of the other types of OPV. IPV needs to be introduced on an accelerated timeline so that OPV type 2 can be withdrawn. IPV should be introduced at least 6 months before the switch from tOPV to bOPV, i.e., by the end of 2015. Countries using only OPV in their routine immunization programmes should be prepared for a switch from tOPV to bOPV in 2016. The countries at highest risk for cVDPV emergence, wild poliovirus transmission and importations of either will be prioritized for earliest IPV introduction. Introducing at least 1 dose of IPV will ensure that a substantial proportion of the population is protected against type 2 polio after OPV type 2 withdrawal. It will also boost immunity to the remaining type 1 and 3 poliovirus serotypes.

Introducing IPV will boost population immunity against polio and mitigate paralysis risks in the case of outbreaks by 'priming' the population against type 2 poliovirus and ensuring better immune responses to OPV if needed. IPV introduction sets the stage for ending OPV use entirely in 2019-2020. In the endgame, polio eradication activities and strengthening routine immunization can be mutually beneficial. IPV will be introduced through routine immunization delivery systems. Strengthening routine immunization is necessary to achieve and maintain high population immunity against polioviruses, especially type 2, after OPV type 2 is withdrawn. The magnitude, number and length of both wild poliovirus (WPV) and cVDPV outbreaks are closely correlated with weaknesses in routine immunization systems.

This is an opportunity for the global polio eradication initiative to use its infrastructure to contribute more systematically to strengthening routine immunization systems. One of the goals is to improve infant routine immunization coverage in a group of focus countries which have some of the lowest routine immunization coverage levels in the world and the greatest proportion of the world's unvaccinated children. The third dose of DTP-containing vaccine will be used to measure routine immunization coverage improvements. Monitoring and detecting wild and vaccine-derived polioviruses and disease will be crucial to the success of endgame strategies.

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