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Universal use of inactivated polio vaccine

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Abstract

Objectives: To present an update on the status of poliomyelitis worldwide, number of cases per year, regions most affected by the disease, vaccines currently available, their risks and benefits, monovalent vaccine use, risks of disseminating a mutant virus in the community, progress that has been made in terms of worldwide eradication and the World Health Organization's (WHO) proposals in this transition period between global eradication and the post-eradication period.

Sources of data: Data for the period from 1955 to 2005 were searched in MEDLINE, LILACS, The Web, Doctor's Guide, WHO website and Pan American Health Organization (PAHO) website and text book.

Summary of the findings: In 1988, the WHO established the goal of eradicating the disease and interrupting transmission of the wild virus globally. Since then, there has been a dramatic decline of the disease, although in 2005 there were still some countries considered endemic and others where polio returned on account of imported viruses. The vaccines used worldwide are the classical tOPV and IPV, and in this eradication process, the use of mOPV vaccines has been encouraged in places where only one type of poliovirus circulates. In addition to spreading the virus in the community, the OPV vaccines may, however, cause paralyses by reversal of the neurovirulence process.

Conclusions: For a world free of poliomyelitis disease, it would be necessary to interrupt circulation of the virus, which will only be possible if the OPV virus were to be discontinued, in accordance with the WHO proposals for this transition period and the post-eradication period.

J Pediatr (Rio J). 2006;82(3 Suppl):S75-82: Poliomyelitis, OPV vaccine, IPV vaccine, eradication of polio, polio epidemic, poliomyelitis, World Health Organization.

Introduction

In May 1988, when approximately 350,000 cases of poliomyelitis occurred in the world, the World Health Organization (WHO) established the goal of eradicating the disease by the middle of the new century and interrupting transmission of the wild virus globally.

In this process, the oral poliomyelitis vaccine (trivalent OPV) played a fundamental role, both because it was easy to administrate, favoring high vaccine coverage rates, and because of greater vaccine virus fecal-oral transmission. Three types of wild viruses, known as type 1, type 2 and type 3, cause poliomyelitis. As part of the initiative for global eradication of the disease, the main weapon against them was the so-called trivalent vaccine (tOPV), synthesized from the three types of live and attenuated viruses. When there is more than one type of virus circulating in one and the same community, tOPV is epidemiologically and operationally the best vaccine to use. When this vaccine is used, however, there is competition among the three types of viruses, and the end result is that it causes protection that is not equally efficient for each type of virus. Protection against polio type 2 is the most easily developed. Wild poliovirus type 2 circulation was interrupted in 1999. At present, only wild polioviruses 1 and 3 circulate in critical areas for the disease (poliovirus type 3 still circulates in India, northeastern Nigeria, Southeast of Niger and Afghanistan).[1]

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Status of poliomyelitis in the world

The WHO resolution to eradicate the disease by the middle of the new century had a dramatic impact on the disease incidence rates. Of the six WHO regions, namely, Africa, America, East of the Mediterranean, Europe, Southeast Asia and the West Pacific, only three of them (Americas in 1994, West Pacific in 2000, Europe in 2002) were able to obtain their eradication certificate, that is, 3 years free of poliomyelitis caused by the wild virus, under a strict system of active epidemiologic surveillance.[2]

Southeast Asia presented a decline of over 94% in the number of cases, that is, from 25,253 cases in 125 countries (polio 1, 2 and 3) in 1988[3] to 1,600 confirmed cases (polio 1 and 3) in 2002 and 225 cases in December 2003.[4] In the beginning of 2005, the number of notified cases of the disease worldwide had been substantially reduced (over 99%), with only six countries still maintaining endemic poliomyelitis from the wild virus (Nigeria and India with the highest number of cases; Pakistan, Niger, Afghanistan and Egypt with a small number of cases). India's example was significant.[5] In 2002 and 2003, this country had the highest number of cases in the world, and Nigeria was ranked second, with 1,517 and 180 cases, respectively. Teamwork by an aware volunteer population enabled thousands of children to be vaccinated, resulting in a substantial decrease in the number of cases in India, to 224 by the end of 2003. In 2004, the number of polio cases in India was 134[5] and, on May 30, 2005, it had fallen to only 15,[4,5] a very encouraging figure achieved in 2 years. In Nigeria, however, religious leaders, claiming that the polio vaccine transmitted the AIDS virus and caused infertility, forced the immunization program to be suspended. As can be imagined, the number of polio cases increased greatly, making it possible for the virus to be exported to various countries in the world. In the beginning of 2005, in addition to the six countries with endemic polio, there were 18 countries with polio from the imported virus. At present, there are more cases of polio from imported viruses than from endemic polio.

In 2003/2004, due to the increased number of cases in Nigeria, with wild virus transmission to other previously poliomyelitis-free countries, a massive vaccination campaign was launched in Africa and Asia. This campaign reached 45 countries, in which 375 million children were vaccinated with tOPV vaccine. These campaigns were intensified in 2005, with the WHO proposal to eradicate the disease by the end of the year. The affected countries are making an effort to eliminate the problem. In April 2005, importation of poliovirus type 1 from Saudi Arabia and the Sudan, countries with extremely low populational vaccine coverage, resulted in an important outbreak in Indonesia, after 10 years without wild poliomyelitis.[6] This was extremely worrying, and emphasized the need for maintaining high vaccine coverage and excellent quality epidemiologic surveillance, in addition to maintaining routine immunization with OPV or IPV. Another country with a significant number of cases on account of poliovirus importation was Yemen. After various actions, with national immunization days with mOPV1, the epidemic is considered under control.[7]

On November 1, 2005, the number of poliomyelitis cases in the world was 1,469[8] (Table 1). It is noted that Egypt no longer appears on this list, although it is still listed as one of the six countries in which wild polio is endemic (Nigeria, India, Pakistan, Niger, Afghanistan and Egypt). After mOPV1 vaccine was used in the campaigns, the last case of wild polio reported in Egypt was in January, 2005. The WHO considers that the main challenge in terms of eradication continues to be Nigeria, requiring some additional months of intensive work to break the transmission chain.[9]

Table 1 - Number of poliomyelitis cases in November 2005

Total number of cases in the world	1,469
Nigeria (endemic)	544
Yemen (importation)	473
Indonesia (importation)	283
India (endemic)	45
Somalia (importation)	37
Sudan (re-established transmission)	26
Pakistan (endemic)	19
Ethiopia (importation)	17
Angola (importation)	9
Niger (endemic)	5
Afghanistan (endemic)	4
Mali (importation)	3
Chad (re-established transmission)	1
Camaroon (importation)	1
Eritrea (importation)	1
Nepal (importation)	1

Types of poliomyelitis vaccines available

The large paralytic poliomyelitis epidemics were controlled thanks to the advent of efficient vaccines that constituted the only means of preventing the disease. There are two types of vaccines available, which differ as regards administration and immunologic mechanism: injectable inactivated poliovirus vaccine and oral attenuated poliovirus vaccine.

Inactivated poliomyelitis vaccine

The inactivated poliovirus vaccine (IPV), developed by Salk in 1954, was the first to be licensed and used initially in the USA. The authors demonstrated that the poliovirus, by incubation with formalin 1/1,000 in a 12 to 14 day

period, at a temperature of 37 ºC, pH 7, became inactivated, but maintained adequate antigenic power.[10]

The first inactivated vaccines containing the three types of poliovirus used monkey kidney cell cultures, a limiting factor for large scale production. Furthermore, for safety, they had their immunogenicity diminished after the Cutter incident, when various cases of paralysis were associated with administration of two lots of incompletely inactivated vaccines.[11] In spite of the considerable impact on the incidence of poliomyelitis, the injectable vaccine was gradually replaced with the oral attenuated poliovirus vaccine. To this day some countries maintain the exclusive use of the inactivated vaccine with good results.

With the advances in cell culture, virus purification and concentration methods, it has become possible to produce highly potent inactivated poliovirus vaccine (eIPV, denominated IPV in this paper) on an industrial scale, with consequent cost reductions. The new vaccine, started at the age of 2 months, is able to provide protective antibody levels with only two doses.[12,13] The immunity developed by the inactivated poliovirus vaccine is essentially of the humoral type. The vaccine does not compete with the wild polio virus at intestinal level. Studies have shown that after parenteral eIPV administration, there is moderate secretory IgA production in the nasopharynx,[14] and experimental studies in monkeys suggest that some degree of immunity is induced at intestinal level, by a mechanism that has not yet been explained.[15]

Because it contains dead viruses, this vaccine immunizes exclusively the vaccinated individual and there is no secondary immunization among contacts. In compensation, there is also no risk of generating mutant viral strains, capable of producing occasional cases of paralysis associated with the vaccine. IPV may, therefore, be used safely in immunosuppressed patients.[16,17]

In our environment, as is the case in most developing countries, routine poliomyelitis vaccination is done with oral attenuated live virus vaccine, the inactivated vaccine being indicated only for individuals who present some contra-indication for receiving oral vaccine.

Basically, IPV is indicated and available in Brazil in the Special Immunobiology Referral Centers (CRIE – Centros de Referência para Imunobiológicos Especiais) for:

- Immunosuppressed individuals in general – primary immunodeficiencies, HIV infection (asymptomatic or symptomatic), neoplasias, immunosuppression, chemotherapy drug or radiotherapy, bone marrow transplant.
- Home contacts of immunosuppressed individuals.

Oral poliomyelitis vaccine

After successive passages in an animal host, Sabin developed attenuated strains of the three types of poliovirus with loss of neurovirulence, maintaining the infection capacity in the gastrointestinal tract, and immunogenic capacity.[18]

Attenuated poliovirus vaccine (OPV) is administered orally, and similarly to infection by the wild polio virus, it produces both local immunity at mucosa level and humoral immunity.[19] Released for use in the USA in 1962, OPV gradually supplanted inactivated poliovirus vaccine (the "old" IPV) thanks to its superiority in terms of immunogenic capacity, the ability to induce local class IgA antibody production in the oropharynx and the gastrointestinal tract, in addition to being low cost and easy to administer.[20]

In addition to the immunity produced, the vaccine virus competes with the wild polio virus to occupy the coupling sites in intestinal lumen, and is therefore very efficient in blocking outbreaks.[21] Vaccination viruses that colonize the intestines are excreted in large quantities in the feces and may secondarily infect the vaccinated individual's susceptible contacts, producing immunity in them as well. The capacity of attenuated strains to spread contributes to a higher rate of immunization than that provided by vaccination coverage.[22] This knowledge provides the basis for mass vaccination campaigns, successfully implemented in various regions of the world.

Attenuated anti-poliomyelitis vaccine may be presented in trivalent (containing the three types of poliovirus), bivalent (containing two types) or monovalent (containing only one type) suspensions, the trivalent form being used for routine immunization.

In the majority of susceptible children who receive oral vaccine, the virus persists in the oropharynx for 1 to 2 weeks and is excreted in the feces for a period of up to 2 months, the excretion peak being in the first week after administration.[23]

As is the case with other live virus vaccines, OPV is thermo-unstable, and great loss of potency occurs through heat. Of the three strains, P_3 is the most thermo-unstable, losing potency some hours afterwards at temperatures above 10 ºC. Therefore, it is fundamental to maintain an adequate cold chain to guarantee the vaccine's full immunogenicity. One of the problems noted with the use of the vaccine is the low rate of seroconversion obtained with oral vaccine administration in tropical countries. Whereas in temperate climate countries over 95% seroconversion is obtained, in tropical climate countries various studies have shown seroconversion rates as low as 50%,[24,25] and additional doses are necessary for seroconversion.[26] A review of oral vaccine immunogenicity studies in developing countries showed that on an average, after three doses of VOP, only 73, 90 and 70% are protected against the polioviruses P_1, P_2 and P_3[27] respectively. Probably, oral anti-polio vaccine thermo-instability,[28] and mainly, the interference of other enteroviruses contribute to this.[29]

There have been recent examples, such as various cases of wild poliomyelitis that occurred in Cape Verde in children vaccinated with three doses of OPV. In India, in 2001, in accordance with WHO reports of 268 confirmed cases of wild polio, 23% had received 4-5 doses of OPV and 36% had received more than five doses of OPV. In addition to these considerations, it is known that intestinal immunity caused by IPV vaccine is less consistent and less lasting than intestinal immunity caused by OPV vaccine. Intestinal immunity that occurs after OPV is serotype-specific, and is more immunogenic for serotype 2.[30] For serotypes 1 and 3, supplementary immunization campaigns with several doses of OPV are required for routine immunization.

Both vaccines provide collective immunity because they diminish wild virus transmission (herd immunity). Herd immunity was well demonstrated, even with the old IPV vaccine, with a lower antigen content.[31,32] As previously explained, however, IPV vaccine does not allow the vaccination virus to be disseminated and OPV vaccine does. This frequently convenient dissemination, in accordance with the epidemiologic situation, may become a problem. And this is exactly what is currently being discussed.

Table 2 - Poliovirus definitions

VAPP	Poliomyelitis from the OPV vaccine Recent exposures to the virus Virologically and epidemiologically independent episodes
cVDPV	Circulating poliomyelitis virus derived from OPV vaccine [≥ 1% of diversity from the nucleotidic sequence of the Sabin strain indicating prolonged replication with or without circulation in (VDPV)]. They can be isolated from healthy individuals or from the environment. They may also occur in **outbreaks** involving a transmission chain by the dissemination of this new specific mutant virus.
iVDPV	Poliomyelitis virus derived from OPV vaccine, in immunosuppressed individuals

cVDPV = Circulating vaccine-derived poliovirus;
iVDPV = Immunodeficient vaccine-derived poliovirus;
VAPP = Vaccine-associated paralytic poliomyelitis.

Risk associated with OPV vaccine use

Although the benefits of OPV vaccine are very well known, some adverse events associated with its use may occur.

The vaccination viruses are derived from wild virus strains with extremely reduced neurovirulence and transmissibility. During replication, the vaccination virus may undergo reverse mutation with increase in neurovirulence, and may cause rare cases of vaccine-associated paralytic poliomyelitis (VAPP) in both vaccinated individuals and non-vaccinated contacts. If, in addition to neurovirulence, transmissibility is also re-acquired, as occurs with the circulating vaccine-derived poliovirus (cVDPV), outbreaks of paralysis associated with the vaccine may occur. The definitions of the events associated with OPV and their causes appear in Table 2.

The main adverse event associate with OPV is post-vaccination paralysis, both in vaccinated individuals and contacts. The risk of paralysis is substantially greater in the first dose of OPV than in subsequent doses. In immunosuppressed individuals, this risk is even higher, around 3,200 times higher than in immunocompetent individuals.[33] A cooperative study conducted by the WHO in 13 countries showed a rate of one case of paralysis associated with the vaccine for each 3.2 million doses distributed, both in vaccinated and contact individuals. Data in the USA estimated one case for 2.4 million doses distributed, the risk being 1/750,000 in the first doses and 1/5.1 million in subsequent doses.[34]

In Brazil, the incidence of poliomyelitis associated with vaccine has been low. Between 1988 and 2003 (15 years), 40 confirmed cases of poliomyelitis associated with oral vaccine were registered, basically in children, with predominance in the first and second doses. The estimated risk in studies on the first dose ranged from one case in 1.2 million to one case in 2.4 million doses applied, and for all the doses, it ranged from one case in 3.6 million to one case in 13 million doses applied.[35]

According to the Pan-American Health Organization (PAHO) and WHO, there are two types of poliomyelitis related to the vaccine:[36]

- Case of poliomyelitis associated with vaccine: Flaccid and acute paralysis that starts between 4 and 40 days after receiving OPV, and that presents neurological sequelae compatible with poliomyelitis 60 days after the onset of motor deficit.
- Case of poliomyelitis associated with vaccine in contacts (those in communication): Flaccid acute paralysis that appears after contact with a child receiving OPV up to 40 days previously. The paralysis appears between 4 and 85 days after vaccination, and should present neurological sequelae compatible with poliomyelitis 60 days after the onset of motor deficit.

In any of the cases, it is imperative to isolate the vaccine poliovirus in stool samples so that the case can be considered associated with the vaccine. The stool sample collection is extremely important as early as possible in the first 14 days after the onset of motor deficit. But even if stool is collected later, between 15 and 40 days after the onset of motor deficit, and vaccine virus is isolated, the case will be considered associated with the vaccine.

All the polioviruses[37] currently isolated are analyzed, and in accordance with their intratypical differentiation, they have been sequenced in accordance with the surface protein of the viral capsid (VP1).[38] Isolates with < 1% of difference from the Sabin strain of the same serotype are classified as Sabin-like; 1 to 15% difference are classified as VDPV (if they circulate and cause outbreaks, they are called cVDPV; if they occur in immunosuppressed individuals, they are called iVDPV; and if isolated from patients without immunodeficiencies and not associated with outbreaks, they are ambiguous aVDPV); and those with over 15% of difference are classified as wild virus.[39] Considering genetic similarities, there is less than 82% similarity between the wild virus and OPV, and more than 99.5% between the VAPP virus and the vaccination virus.

The excreted viruses that are derived from vaccines are frequently more virulent than the original OPV strains. During excretion, mutations and genetic alterations occur rapidly, in a sequential manner, in response to the different intestinal pressures. Low levels of immunity in the population favor the selection and transmission of vaccine variants with biological properties that are undistinguishable from those of the wild polioviruses.[40-42]

As a result of this, a type of virus currently known as cVDPV appeared, that is, a circulating poliomyelitis virus derived from the vaccine. It can be isolated in healthy and immunosuppressed individuals, and from the environment. The cVDPV is implicated in outbreaks involving a transmission chain by a specific mutant virus. For example, the poliomyelitis outbreaks that occurred in China during the 1990s, due to OPV2, and more recently, in 2004, two cases; the polio outbreak in Egypt from 1988 to 1993 (32 cases; 93 to 96% genetic similarity to OPV2); the polio outbreak in Hispaniola (Dominican Republic and Haiti) in 2000/2001 (31 notified cases; 97% genetic similarity to OPV1) and three cases in the Philippines (97% similarity to OPV1) in 2001, in addition to four cases in Madagascar in 2002, and in China in 2004.[43] The outbreak in Hispaniola received great attention in the medical literature,[44] and wide coverage and publicity in the press. Low vaccine coverage favored conditions for the development of cVDPV outbreaks.

Although generally associated with outbreaks, VDPV may be isolated in individuals who are either immunosuppressed or not, occasionally or not, without the occurrence of outbreaks. The recent example in the USA is noted, in which the VDPV virus was isolated in four non-vaccinated Amish children from a case index with immunodeficiency. The viruses isolated were derived from the Sabin poliovirus type1 strain, with 97.7% genetic similarity.[45] Lack of population vaccine coverage favors dissemination of the viruses (as in the case of Hispaniola, in which coverage was around 30 to 60% in 2000[44]), and this explains why an outbreak has not occurred in the USA, at least up to the present time. It is important to emphasize that in the USA, the vaccination schedule against poliomyelitis has used exclusively eIPV since 2000, and since that time there has not been any case of VAPP.[46]

It is estimated that mutation occurs in the range of 1% per year, which indicates that the circulation time for cVDPV can be inferred from the degree of divergence in the genetic sequence.[37] Failures in vaccination coverage are critical determinant factors in the occurrence of cVDPV outbreaks.[38] In accordance with recent WHO publications,[8] of the 333 confirmed polio cases in Southeast Asia up to November 2005, 31 were from viruses derived from OPV vaccines, and of the 528 confirmed cases in Africa, four were from viruses derived from OPV vaccines.

Another problem to be faced is poliovirus maintenance in immunosuppressed individuals (iVDPV), as potential reservoirs, with permanent excretion of the viruses (which can be over 6 months in a person with severe primary immunodeficiency).[46] Theoretically, the iVDPV could reintroduce the poliovirus in the general population. In 40 years of OPV use, however, 28 iVDPV were documented up to the end of 2004, including one in Thailand in 2003, without the occurrence of secondary cases. In four of these cases (all isolated in developed countries), excretion was prolonged for over 36 months. On this particular issue, there is also concern about environmental contamination by vaccination poliovirus (for example, in the water and sewage networks).[47]

Continuity of OPV use in the public health context

The WHO estimates that with the eradication of the wild poliovirus from the world, initially forecast for the end of 2005, or at a time very close to this, the continued use of OPV vaccine would compromise the proposal of a poliomyelitis-free world. This is easy to understand. It is estimated that the number of VAPP cases will continue to occur in the proportion of two to four cases per million births, leading to around 250 to 500 new cases of VAPP per year. The WHO estimates that the major occurrence of VAPP should occur in India with a rate of two cases per million births.[43] As regards outbreaks from cVDPV, more than one outbreak per year is estimated with the continuation of OPV.[6]

Thus, the continued use of OPV after interrupting the wild virus circulation and transmission, becomes inconsistent with a world free of polio and its eradication.

Until global certification of wild polio eradication is obtained, there must always be vaccination, either with OPV or eIPV. Vaccination coverage must be maintained in the routine schedules and in some cases supplementary immunization activities, such as vaccination campaigns, mop-up campaigns, etc.

As a strategy to eradicate wild polio from places where it still occurs endemically or from imported viruses, the WHO has encouraged the development and application of monovalent OPV vaccines (mOPV).[1,48] Studies have shown that with the same number of doses, mOPV vaccine leads to greater type-specific immunity when compared with tOPV. For example, in tropical countries, while 80 and 72% of the children develop immunity with mOPV1 and mOPV3, only 40 and 31%, respectively, develop immunity with tOPV for poliovirus type 1 and for poliovirus type 3[1] after the first dose, which represents a great advantage, since the large majority of wild poliomyelitis cases occur in children under the age of 2 years. An additional advantage is that if children immunized with mOPV are later exposed to the wild virus (of the vaccine serotype), it is expected that 40% will excrete less virus for a shorter period of time, thus limiting the possibility of later transmission.

The recent introduction of mOPV1 would seem to have interrupted transmission in two technically problematic areas of eradication in the world – Egypt and many areas of India.[7] mOPV1 was first used in April 2005 in India and subsequently in Egypt.[48] The WHO has recommended the expanded use of mOPV in mop-up campaigns, including in countries affected by outbreaks, such as Indonesia, Yemen, Ethiopia, Somalia and Angola.[7]

IPV vaccine use

The great advantage of IPV vaccine is its excellent efficiency and safety profile. As far as individual protection is concerned, IPV vaccine does not cause paralytic poliomyelitis, VAPP or predisposition to the appearance of VDPV. It may be associated with other vaccines in what is called combined vaccines, providing greater comfort, convenience and adhesion. In addition, no supplementary doses are required in the primary vaccination schedule, thus reducing the cost of innumerable vaccination campaigns, such as those that accompany OPV vaccine.

At present there are 22 countries in the world that routinely apply only IPV vaccine in their primary vaccination schedule. These include the USA, Canada, England and the majority of European countries. Of these 22, four maintain one booster dose with OPV. Another seven European countries have a sequential schedule with two initial doses of IPV, followed by two doses of OPV.

The great disadvantage of IPV in the polio eradication context is that there is a limited annual production capacity, which perhaps does not exceed 100 million doses.[49] Production could be increased and the price per dose could fall, if the manufacturing laboratories could be given guarantees that there would be an international consumer market for billions of doses of IPV to be produced in the post-vaccination era.[49]

Simultaneous cessation of OPV vaccine use

As a result of the above-mentioned facts, world public health authorities and the various countries in tandem with the WHO are currently discussing the eventual simultaneous global cessation of OPV, after the global eradication certificate is obtained (3 years without poliomyelitis, maintaining epidemiologic surveillance at levels recommended by the WHO). The end objective of the WHO Polio Eradication Initiative[6] is to assure that transmission of the poliovirus is globally interrupted through nationally and internationally coordinated action, leading to humanitarian and economic benefits from this eradication.[6] There are various publications about the subject which deserve very special attention from the entire medical community.[2,50]

The main challenges for a polio-free world are to break the final transmission chains in endemic countries, to control outbreaks in countries previously free of the wild virus, to maintain funding and political commitment, to control the problem of low vaccination coverage in polio-free countries and to assure that sufficient stocks of vaccine are maintained.[51]

Differently from the anti-smallpox vaccine, the eventual cessation of OPV use must be synchronized throughout all the countries that use it. But cessation of OPV also involves risks, summarized as follows:[43]

- The immediate risk of cVDPV emergence – this risk would be greater in the first few months and would be lower in countries with high vaccination coverage at the time of OPV cessation, and if the countries were perfectly coordinated for simultaneous cessation. The risk is estimated at 65 to 90% in the first year after simultaneous OPV cessation, dropping to 5 to 15% in the second year, with reduction to 1 to 5% at the end of the third year.
- The medium and long-term risk of re-introducing poliovirus originating from stocks of any nature (diagnostic laboratory, for example). This risk is small, if biological material is adequately contained. Even with poliovirus derived from iVDPV, the risk is very low.

Although they are slight, these risks do exist. Thus, the WHO proposal to implement strategies that must comply with a schedule are justified.[52] There are six prerequisites for this simultaneous cessation (WHO):

- Confirmation that global transmission of wild poliovirus has been interrupted;
- Appropriate containment of biological material containing poliovirus;
- Maintenance of international stocks of mOPV vaccine (to control eventual outbreaks in the simultaneous OPV cessation phase);

- Maintenance of active, high quality, epidemiologic surveillance of circulating poliovirus;
- Simultaneous, duly coordinated cessation of OPV;
- Establish a long-term, routine national immunization policy with IPV, depending on the decision of every country.

For the countries that use OPV routinely in public health immunization (even if they also use IPV in combined vaccines, in immunization through private clinics), the priorities at this preparatory stage for global cessation of OPV may be pointed out as follows:[43,52]

- To reinforce active epidemiologic surveillance of flaccid acute paralysis, to certify eradication, for eventual detection of wild poliovirus and/or cVDPV and to detect the potential appearance of imported poliovirus.
- Implement appropriate contention of wild poliovirus and poliovirus derived from OPV vaccine. Develop stocks of mOPV and criteria for its use.
- Maintain high vaccination coverage (> 90%), minimizing the risk of transmission of imported and/or emergency cVDPV or VDPV viruses (this vaccination coverage must be with OPV or IPV, depending on the country's immunization policy).
- Decide, after analyses of risks, benefits and costs, when to interrupt all routine poliomyelitis immunization after OPV cessation (at this time, the IPV vaccine will be the only option available for routine immunization). The WHO recommends that countries that decide to continue with their routine immunization with IPV, after global OPV suspension, in addition to analyzing costs and benefits, should take various factors into account, such as the impact on the schedule and control of other diseases, alteration of the pertussis component in combined vaccines, use of the vaccine with a different preservative, among other operational problems as a result of this measure.
- Make an estimate of the risks of iVDPV and establish a plan to control it, if necessary.
- Prepare national plans and mechanism for cessation of all OPV used in routine immunization programs, in addition to destroying remaining stocks of tOPV.

These priorities must comply with a certain sequence, that is, it is estimated that the post-OPV era should be reached in 6 to 8 years time.[52]

Final considerations

The poliomyelitis type 1, 2 and 3 viruses currently in circulation, derived from OPV, constitute a threat to a completely poliomyelitis-free world. With polio eradicated, the trend is to reduce vaccination through carelessness, or because there are other priorities that deserve immediate attention. If some countries continue to use OPV, the virus will continue to circulate, undergo mutations and will find unprotected populations on a larger or smaller scale, depending on the vaccination coverage of that group. Therefore outbreaks of cVDPV will appear, as we have already seen in various places in the world, and the problem of poliomyelitis will not be solved.

The operational difficulty of implementing IPV vaccine, because it is parenteral, in addition to the cost associated with it, are the reasons given for not adopting it as routine in immunization programs of developing countries. Perhaps the use of combined vaccines may make it feasible to implement IPV vaccine, especially if we think of the enormous cost of OPV campaigns and the loss of vaccines that is known to occur. The time has come for us to schedule a change in the poliomyelitis vaccination policy.

To sum up, eliminating poliomyelitis disease ultimately requires suspension of the circulating virus. And when there is no longer any wild poliomyelitis in the world, the only circulating virus will be the OPV vaccine, which must be discontinued.

Yes, it is only under these conditions that we will finally be able to have a poliomyelitis-free world!

Conflict of interest

Luiza Helena Falleiros Carvalho declares that she is a member of the speaker's bureau for Glaxo SmithKline, Sanofi-Pasteur, Pfizer, and Wyeth Laboratories.

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