Eradicating Polio: How the World’s Pediatricians Can Help Stop This Crippling Illness Forever

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The American Academy of Pediatrics strongly supports the Polio Eradication and Endgame Strategic Plan of the Global Polio Eradication Initiative. This plan was endorsed in November 2012 by the Strategic Advisory Group of Experts on Immunization of the World Health Organization and published by the World Health Organization in April 2013. As a key component of the plan, it will be necessary to stop oral polio vaccine (OPV) use globally to achieve eradication, because the attenuated viruses in the vaccine rarely can cause polio. The plan includes procedures for elimination of vaccine-associated paralytic polio and circulating vaccine-derived polioviruses (cVDPVs). cVDPVs can proliferate when vaccine viruses are transmitted among susceptible people, resulting in mutations conferring both the neurovirulence and transmissibility characteristics of wild polioviruses. Although there are 3 different types of wild poliovirus strains, the polio eradication effort has already resulted in the global elimination of type 2 poliovirus for more than a decade. Type 3 poliovirus may be eliminated because the wild type 3 poliovirus was last detected in 2012. Thus, of the 3 wild types, only wild type 1 poliovirus is still known to be circulating and causing disease. OPV remains the key vaccine for eradicating wild polioviruses in polio-infected countries because it induces high levels of systemic immunity to prevent paralysis and intestinal immunity to reduce transmission. However, OPV is a rare cause of paralysis and the substantial decrease in wild-type disease has resulted in estimates that the vaccine is causing more polio-related paralysis annually in recent years than the wild virus. The new endgame strategic plan calls for stepwise removal of the type 2 poliovirus component from trivalent oral vaccines, because type 2 wild poliovirus appears to have been eradicated (since 1999) and yet is the main cause of cVDPV outbreaks and approximately 40% of vaccine-associated paralytic polio cases. The Endgame and Strategic Plan will be accomplished by shifting from trivalent OPV to bivalent OPV (containing types 1 and 3 poliovirus only). It will be necessary to introduce trivalent inactivated poliovirus vaccine (IPV) into routine immunization programs in all countries using OPV to provide population immunity to type 2 before the switch from trivalent OPV to bivalent OPV. The Global Polio Eradication Initiative hopes to achieve global eradication of polio by 2018 with this strategy, after which all OPV use will be
BACKGROUND

Before eradication efforts began, polio was a pervasive viral disease and a significant cause of disability. Polio is highly contagious and may be caused by 3 serotypes of poliovirus: types 1, 2, and 3. The virus is transmitted person-to-person through several routes: fecal-oral, oral-oral, and, rarely, through a common agent such as water or milk. In industrialized countries, oral-oral transmission is thought to predominate, whereas in developing countries with poor sanitation and hygiene, fecal-oral transmission is believed to be the major mode of spread. The period of communicability typically lasts approximately 4 weeks and can last up to 8 weeks, although most transmission occurs in the first 7 to 14 days with excretion from the oropharynx and peak stool titers. Onset of first symptoms (typically fever, malaise, drowsiness, headache, nausea, vomiting, constipation, or sore throat, in various combinations) occurs 3 to 6 days after infection and onset of paralytic disease occurs 7 to 21 days (range: 3–35 days) after infection.1 Paralytic disease occurs in <1% of unvaccinated children infected by the virus (generally ranging by serotype from 1 in 200 infections to 1 in 2000 infections; type 1 is the most neurovirulent and type 2 the least neurovirulent).2 Case fatality rates among people with paralytic disease range from 5% to 10% and are variable by region as well as by age groups. Two poliovirus vaccines, inactivated and oral, have been used to protect many millions of children and achieve elimination of polio in most countries in the world. Inactivated poliovirus vaccine (IPV), developed by Jonas Salk and first licensed in the United States in 1955, protects against viremia and paralysis from all 3 virus types. IPV is the vaccine (as a more potent preparation) currently used in the United States and most industrialized countries because of its safety profile (see Statement of Problem section).3 Oral polio vaccine (OPV) is a live-attenuated vaccine developed by Albert Sabin. Trivalent OPV (tOPV), which contains attenuated strains of all 3 serotypes, was first licensed in the United States in 1963. OPV is the vaccine used in most developing countries because of its lower cost, better inducement of intestinal immunity than IPV, and ease of administration through oral drops.1 The type 2 component of tOPV inhibits seroconversion to the other serotypes, requiring multiple doses to induce high levels of protection to all 3 serotypes. To enhance per-dose immunogenicity against serotypes 1 and 3, other formulations of OPV have been developed: monovalent (mOPV) for types 1 or 3 and bivalent (bOPV), containing attenuated viruses of types 1 and 3.4–6 Most industrialized countries now use IPV, which provides high levels of systemic immunity preventing viral invasion of the central nervous system and high levels of oropharyngeal protection, thereby diminishing the main mode of spread in these countries. OPV remains the major vaccine for achieving eradication of wild polioviruses in developing countries because it induces high levels of intestinal immunity to prevent fecal-oral spread, superior to the levels of intestinal immunity induced by IPV. The use of both IPV and OPV vaccines dramatically decreased polio incidence in the United States within just a few years and throughout the world in a few decades. Since the resolution by the World Health Assembly in 1988 to eradicate polio, tremendous progress has been made, with a >99% reduction in the annual number of cases. Type 2 polio, caused by wild viruses, appears to have been eradicated, with the last naturally occurring case detected in Aligarh, India, in 1999. Type 3 wild poliovirus also appears to be on the verge of eradication, with the last case detected in November 2012 (as of October 28, 2014).7 These major achievements were accomplished primarily through the use of tOPV and, more recently, bOPV and mOPV. Only 3 countries (Pakistan, Nigeria, and Afghanistan) have never interrupted wild poliovirus transmission and are considered endemic areas and reservoirs for transmission of viruses to areas that have been free of wild poliovirus. Polio cases in 2 of the 3 endemic countries (Afghanistan and Nigeria) decreased by 57.9% in 2013 compared with 2012, whereas Pakistan experienced a 60.3% increase. Wild poliovirus type 1 from Nigeria has been exported into the Horn of Africa involving 3 countries (Somalia, Kenya, and Ethiopia); another type 1 virus from Nigeria is causing an outbreak in
Cameroon, and virus originating from Pakistan has led to an outbreak in Syria. Somalia, the epicenter of the outbreak in the Horn of Africa, had been free of polio since 2007. Furthermore, virus traced to Pakistan has been imported, potentially through Egypt into Israel, where virus was detected starting in 2013 and lasting for more than a year, based on environmental surveillance of sewage samples throughout the country (and in the West Bank and Gaza Strip) as well as in stool surveys. No cases of paralysis attributable to polioviruses had been reported as of October 28, 2014. Since February 16, 2014, no wild polioviruses have been detected in Israel.\(^\text{7}\) Moreover, cases have been detected in 2014 in Equatorial Guinea (linked to Nigerian virus) and Iraq (linked to Pakistan virus), both previously polio free for more than a decade.\(^\text{7}\) Virus genetically related to viruses found in Equatorial Guinea was detected in sewage near an airport in Sao Paulo, Brazil, but no spread within the Brazilian population has been reported. Thus, as long as polioviruses circulate anywhere, all countries are at risk of reintroduction and resultant epidemics of paralysis.\(^\text{6}\)

The main strategies used to achieve polio elimination to date have included the following: (1) delivery of tOPV through routine immunization programs, (2) disease surveillance to detect where virus is circulating, (3) supplemental immunization activities (including national and subnational immunization days, usually at least twice per year, now using mOPV and bOPV, in which mass vaccination campaigns are conducted throughout a specific region in a short interval, usually targeting all children <5 years of age, regardless of previous immunization status), and (4) mop-up campaigns in areas with sustained transmission.\(^\text{9}\) Sometimes, depending on poliovirus epidemiology, people older than 4 years are targeted.

Four of the 6 World Health Organization (WHO) regions have been certified as polio free: the Americas in 1994, the Western Pacific Region in 2000, the European Region in 2002, and the South East Asia Region in March of 2014. India, once a major reservoir, has now gone more than 3 years without detection of wild polioviruses and has been declared wild poliovirus free. India’s achievement was seen as a milestone that put global eradication within reach. India’s accomplishment was aided by modern strategies that included intensive communication and social mobilization, engaging influencers including religious leaders, media advocacy for mass campaigns, and coordinating these strategies to maximize efforts and investment, an approach that should be feasible to remaining endemic countries. Leaders also ensured that high-quality vaccinators were hired, trained, and appropriately supervised; instituted independent monitoring of vaccinator performance; and conducted careful microplanning to ensure that all high-risk areas were covered in supplemental immunization activities.\(^\text{10}\)

The global eradication program for polio has been ongoing since 1988 and has missed 2 previous deadlines for eradication. Currently, achieving eradication is closer than ever, and the year 2012 was an important crossroads for the eradication program: the WHO and World Health Assembly declared polio eradication a public health emergency, and all 3 remaining endemic countries implemented national emergency action plans that resulted in significant improvements in immunization campaign quality. As of October 28, 2014, further reductions in numbers of cases were reported in Nigeria. Pakistan accounts for 86% of the total cases reported to date in 2014.

**STATEMENT OF PROBLEM**

**Eliminating OPV**

To complete eradication of all polio disease, it will be necessary to stop the use of OPV globally, because the live-attenuated viruses can cause polio themselves, albeit rarely.\(^\text{11}\) Sabin vaccine viruses can lead to polio disease in 1 of 2 ways: direct paralysis of vaccine recipients or their close contacts, resulting in vaccine-associated paralytic polio (VAPP), or by acquiring mutations during prolonged circulation in communities with low immunization levels that confer the transmissibility and neurovirulence properties of wild viruses, leading to polio outbreaks from these circulating vaccine-derived polioviruses (cVDPVs).\(^\text{12}\) VAPP is caused by polio vaccine viruses that are closely related genetically to the parent Sabin vaccine viruses but have become neurovirulent, causing disease in actual vaccine recipients or their close contacts. cVDPVs are genetically more distant from the present Sabin viruses than the viruses that cause VAPP. Originally, the global strategy was to eradicate all 3 wild polio serotypes and then stop all use of tOPV. However, the following several factors point to a much-needed change in endgame strategy:

1. type 2 wild poliovirus’ apparent eradication;
2. type 2 poliovirus in OPV interferes with the induction of immunity to types 1 and 3, and bOPV containing only types 1 and 3 induces significantly higher levels of seroconversion to those types than does tOPV;
3. type 2 poliovirus now accounts for approximately 40% of VAPP;
4. type 2 cVDPVs now account for 98% of cVDPVs detected since 2012, and response to these type 2 cVDPV outbreaks can lead to a diversification of resources from efforts to terminate transmission of wild types 1 and 3;\(^\text{7,13}\) and
5. vaccine-derived poliovirus cases have and are expected to continue to exceed wild poliovirus cases (Fig 1).
Thus, to eliminate cVDPVs along with wild poliovirus, the polio endgame now calls for the introduction of IPV in countries that previously used only OPV and a stepwise elimination of OPV types starting with the type 2 component of tOPV in 2016, followed by withdrawal of all OPV in 2019–2020, after the global certification of polio eradication.

**bOPV as a New, Interim Strategy**

Switching to bOPV, which protects against poliovirus types 1 and 3, will stop future generation of type 2 cVDPVs and improve seroconversion and immunity against types 1 and 3 because bOPV is substantially more immunogenic per dose against those serotypes than is tOPV. However, this strategy will leave populations in developing countries vulnerable to type 2 outbreaks from a number of potential sources: continuing circulation of current type 2 vaccine viruses in low-coverage populations or residual use of tOPV in some areas before the supply is exhausted, resulting in transmission of type 2 vaccine viruses among susceptible people, where viruses can mutate, leading to generation of new cVDPV outbreaks; a break in laboratory containment of type 2 viruses, as occurred in India in 2002–2003; or from reseeding of the population by immunodeficient individuals who are chronically shedding virus.*

Otherwise, there is no short-term change in schedule or administration of OPV, just an eventual switch of the kind of OPV being used in routine immunization and campaigns from tOPV to bOPV.

**IPV as “Insurance”**

To reduce the risk of reemergence of paralytic disease resulting from poliovirus type 2 infections and boost immunity to poliovirus types 1 and 3, potentially hastening polio eradication, the WHO Strategic Advisory Group of Experts (SAGE) on Immunization has recommended that all routine immunization programs administer at least 1 dose of IPV before the global switch from tOPV to bOPV in all OPV-using countries. This approach of using ≥1 doses of IPV will provide protection against paralysis should type 2 polioviruses reemerge by inducing some immunity to type 2 in the population. The use of IPV in routine immunization will facilitate outbreak control when used along with mOPV should polioviruses be reintroduced from any source. Data from Faden et al indicate that a dose of IPV followed by a dose of OPV will lead to higher immunity levels than a single dose of OPV, thus facilitating outbreak control compared with controlling an outbreak in an unvaccinated population. Furthermore, when administered to children who have received previous doses of OPV, IPV leads to higher than expected seroconversion rates among seronegative people than when IPV is given to vaccine-naive individuals. Data indicate that IPV is inferior to OPV in reducing oral shedding of viruses and thus should reduce oral-oral transmission of polioviruses. However, IPV is inferior to OPV in reducing shedding of virus in the stool, raising concerns about its effectiveness in reducing transmission via the fecal-oral route, thought to be the predominant mode of transmission in developing countries. Nevertheless, IPV substantially reduces duration of excretion and quantity of virus shed in the stool of vaccinated people compared with vaccine-naive controls, suggesting that it could impede transmission. However, given the inferior intestinal immunity induced by IPV compared with OPV, stockpiles of mOPV will be maintained to contain an outbreak should polioviruses be reintroduced.

**NEW INFORMATION**

**Global Polio Eradication Initiative: A New Strategic Plan**

The Global Polio Eradication Initiative (GPEI) was launched in 1988 and spearheaded by national governments, the WHO, Rotary International, the US Centers for Disease Control and Prevention, and the United Nations Children’s Fund. The GPEI published its new Polio Eradication and Endgame Strategic Plan in April 2013 after endorsement in November 2012 by SAGE. The new endgame plan includes tOPV withdrawal as 1 of 4 primary objectives:

1. detect and interrupt all wild poliovirus transmission by the end of 2014;

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*Research is underway to develop antiviral drugs in hopes of helping these individuals clear the viruses that chronically infect them.
2. strengthen immunization systems, including (a) introduce at least 1 dose of IPV by the third quarter of 2015 (at 14 weeks of age or at first contact thereafter) and (b) replace tOPV with bOPV by 2016 and eventually withdraw all OPV by 2019 (after meeting objective 3); 
3. contain poliovirus and certify eradication; and 
4. plan polio’s legacy (ongoing). 

The GPEI will work with Gavi, the Vaccine Alliance (formerly The Global Alliance for Vaccines and Immunization) and other immunization partners to secure funding, develop adaptive strategies, foster political will, and ensure progress on this endgame plan. As part of the effort to prepare for tOPV withdrawal, the plan outlines how the development and licensure of affordable IPV options will be fast-tracked. This plan includes exploring a new fractional (approximately one-fifth) dose delivered intradermally, adjuvanted IPV formulations that are dose sparing, Sabin IPV formulations that allow production by developing country vaccine manufacturers, and possibly new delivery technologies (eg, via dose-sparing microneedle administration). An overview and the full endgame plan can be found at http://www.polioeradication.org/Resourcelibrary/Strategyandwork.aspx.20

CONCLUSIONS

The Polio Eradication and Endgame Strategic Plan calls for an ambitious objective by asking the more than 120 industrialized and developing countries currently using tOPV to introduce at least 1 dose of IPV in their routine immunization programs by 2015. It also calls on those countries to stop using OPV in a phased manner, beginning with the global switch from tOPV to bOPV in 2016. All international OPV manufacturers will stop tOPV distribution when the coordinated switch from tOPV to bOPV occurs. A current goal of the endgame plan to build political support is to obtain a World Health Assembly resolution of the 193 member states to endorse the switch from tOPV to bOPV and incorporate at least 1 dose of IPV into routine schedules. Without introducing IPV, countries will have an unprecedented accumulation of all children born after the switch who are susceptible to type 2 polioviruses should they be reintroduced. Switching to bOPV without introducing IPV would increase the risk of major outbreaks caused by type 2 polioviruses (cVDPVs or wild virus from breaks in laboratory containment).

Eliminating polio in the remaining endemic countries will ease burdens and free up resources for these countries to focus on other areas of development, both health-related and other areas. Because routine use of IPV is expected to boost immunity to poliovirus types 1 and 3, if IPV is incorporated into the routine immunization programs in these endemic countries soon, it could hasten eradication of those types. 

SAGE Recommendation

In November 2012, SAGE endorsed the 4 major objectives and milestones in the new strategic plan. SAGE also recommended that all countries should introduce at least 1 dose of IPV in their routine immunization programs to mitigate the risks and consequences associated with the eventual withdrawal of the poliovirus type 2 component of OPV.16

Timing of IPV Dose

More recently, in November 2013, among other recommendations, SAGE recommended that IPV be administered in addition to the 3 to 4 doses of OPV in the primary series and that the IPV dose should be administered during an immunization contact at or after 14 weeks of age.21

SUPPORTING AND IMPLEMENTING THE PLAN

A number of obstacles and barriers must be overcome to fully implement the endgame strategic plan and achieve sustained eradication, as follows:

1. increased cost: the United Nations Children’s Fund has reported that IPV will cost approximately $1 per dose for Gavi-eligible (ie, low-income) countries and $2 to $3 for middle-income countries, whereas tOPV costs $0.15 to $0.20 per dose; 
2. administration infrastructure: IPV is administered by injection and thus harder to administer in many global health settings than the orally administered tOPV drops; 
3. strain on cold-chain infrastructure: IPV will be a significant burden because of increased cold-chain storage requirements and is freeze-sensitive; and 
4. inferior intestinal immunity: although IPV induces intestinal immunity, it is inferior to that induced by OPV, causing some concern about IPV use in protecting the population from polio outbreaks in some settings.22

Until eradication is achieved, we will always be at risk for poliovirus reappearing anywhere in the world. The recent experience in Israel underscores the importance of having an early warning system, such as routine sewage testing for poliovirus, for timely detection of virus presence or spread, particularly in countries at high risk of transmission. The continuation of support for overall polio eradication via the GPEI has been deemed justified from an economic perspective.23 The savings from polio eradication come not only from not treating polio cases and the lifelong disability often encountered.
by people with polio but also from discontinuing the current intensive polio vaccination mass campaigns. Since April 2013, GPEI and the Gavi Alliance have been collaborating through the Immunization Systems Management Group to manage and coordinate partners’ activities to achieve introduction of IPV and the tOPV to bOPV switch in the outlined time frame. These activities include a multifaceted strategy to ensure an adequate supply of affordable IPV; financial support for IPV introduction, regulatory requirements, advocacy, and communications; strengthening routine immunization; and country readiness for introduction of IPV into routine immunization systems. More information on these activities can be found at http://www.who.int/immunization/diseases/poliomyelitis/inactivated_polio_vaccine/en/.

In 2013, scientists and technical experts from 80 countries signed the Scientific Declaration on Polio Eradication, which is an endorsement of the strategic endgame plan and a reminder of the consequences of aiming for polio control instead of eradication: at this point, we could expect up to 200,000 cases annually within a decade if the polio eradication effort is stopped, effectively reversing progress made over the past 25 years.24,25 The declaration can be found at http://vaccines.emory.edu/poliodeclaration/text.pdf24 and the list of signatories can be found at http://vaccines.emory.edu/poliodeclaration/signatories.html.

The American Academy of Pediatrics supports the SAGE recommendations and encourages other pediatric societies in middle- and lower-income countries and leading scientists to support the policy and advocate with governments to implement the recommendations. Pediatricians in the United States can help ensure that the US legacy of eliminating polio is sustained and enjoyed by all countries in these important ways (recently updated guidance is underlined):

- Strive to educate parents and patients about the importance of eradicating polio, not just in the United States but worldwide.
- Ensure that patients are vaccinated against polio.
- **Ensure that patients traveling internationally receive all recommended vaccines, including a booster dose of IPV when appropriate** (eg, those at increased risk because of travel to polio-endemic or -epidemic areas of the world, working in a laboratory handling poliovirus, or health care workers treating those with polio)27; moreover, patients traveling internationally should be adequately counseled on the increased risks of contracting illnesses in endemic countries as well as recommended avoidance measures (eg, hand washing).

Centers for Disease Control and Prevention recommendations on polio vaccination:
- **General:** http://www.cdc.gov/VACCINES/vpd-vac/polio/default.htm
- **For travelers:** http://wwwnc.cdc.gov/travel/yellowbook/2014/chapter-3-infectious-diseases-related-to-travel/poliomyelitis
- **For immigrants:** http://www.cdc.gov/immigrantrefugeehealth/laws-regs/vaccination-immigration/revised-vaccination-immigration-faq.html

- **Consider polio in the differential diagnosis of children presenting with fever and acute flaccid paralysis.** If the case is clinically compatible with polio, notify public health authorities immediately and collect 2 stool specimens at least 24 hours apart within 14 days of onset of paralysis for detection of virus. Note that because most polio infections are silent, a case of paralytic polio in the United States may have been acquired from an asymptomatic individual, so a history of travel to a polio-infected area may be absent in the case of paralysis.
- Advocate with government officials about the importance of funding, support, and technical assistance for global immunization programs, especially the GPEI.
- Advocate with pediatric societies in developing and middle-income countries to support incorporation of at least 1 dose of IPV to complement OPV used in routine immunization programs.
- Work with local Rotary Clubs (https://www.rotary.org/en/end-polio) or volunteer with the United Nations Volunteers Program to support polio eradication.

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Pediatrics 2015;135;196; originally published online December 29, 2014;
DOI: 10.1542/peds.2014-3163

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