

FOCUS ON RESEARCH

The Bumpy Road to Polio Eradication

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Related articles, p. 2351 and p. 2360

The existence of poliomyelitis in the developing world was ignored for many years because epidemic polio was considered a disease of wealthier countries. In the 1960s and 1970s, however, “lameness surveys” of schoolchildren in more than 20 countries revealed lower-limb–paralysis rates of 2 to 11 per 1000 — higher than those of the peak polio-epidemic years in the United States.¹ Inspired by the success of global smallpox eradica-

tion and poliomyelitis control in the Americas, the World Health Assembly made a commitment in 1988 to eradicate polio by 2000. Although this goal was not met, substantial gains were made through routine immunization of infants with trivalent oral poliovirus vaccine (tOPV), supplemental national or regional rounds of tOPV among young children, active surveillance for acute flaccid paralysis, and rapid response to disease outbreaks. By 2000, annual reports of poliomyelitis cases had fallen by more than 99%, to fewer than 1000; continuous endemic transmission was halted almost everywhere; and the extinction of

infection with type 2 wild-type poliovirus (WPV) proved that eradication was possible. In the past decade, however, persisting reservoirs of naturally occurring (wild-type) poliomyelitis have proven stubbornly resistant to control, for various reasons — in Pakistan and Afghanistan, because of international conflict; in India, because of an overwhelming force of infection and high rates of failure of oral poliovirus vaccine (OPV)

about a year later and most infection was contained, ongoing transmission of WPVs in northern Nigeria and flares of disease elsewhere have led to periodic exportation of type 1 and type 3 polioviruses to many locations in sub-Saharan Africa and Asia, where immunity levels are insufficient to prevent the spread of infection (see Figure 1). Endemic transmission has been re-established in Chad and Angola, and the newest battlefield is central Asia, where a large outbreak of disease caused by type 1 poliovirus of Indian origin has erupted in western Tajikistan, causing more than 150 cases to date.

But perhaps the biggest bump in the road has been the emergence of circulating vaccine-derived polioviruses (cVDPVs), genetically unstable Sabin-strain viruses that revert toward the genotypic and phenotypic profile of the virulent parent strain as they circulate for extended periods in a population with low immunity levels.² By definition, cVDPVs have acquired mutations in more than 1.0% of the RNA genome coding for the viral capsid protein VP1, and most isolates have undergone recombination with other group C enteroviruses, which may enhance viral fitness. The existence of cVDPVs was discovered in 2000 during an investigation of 21 cases of paralytic type 1 poliomyelitis on Hispaniola. Since that time, one or two cVDPV outbreaks have been reported per year (Figure 2 shows

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associated with overcrowding, poor sanitation, and diarrheal disease; and in Nigeria, because of a poor public health infrastructure and, until recently, lack of political will resulting in very low routine immunization rates and ineffective supplemental immunization activities. In 2003, polio-immunization activities were halted in northern Nigeria owing to false rumors about adverse effects of OPV; the ensuing eruption of disease in a dense population with a high birth rate led to the spread of type 1 polioviruses to about 20 previously polio-free countries in Africa, the Arabian peninsula, and Asia. Although immunization resumed

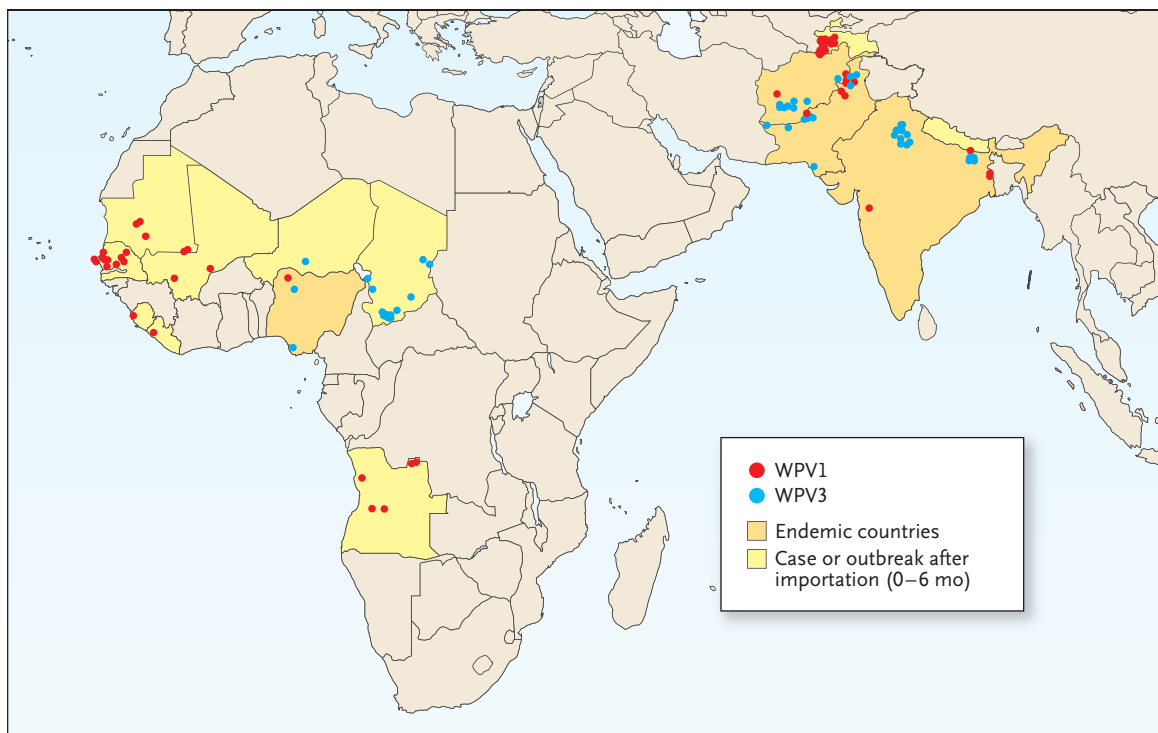


Figure 1. Global Distribution of Wild-Type Poliomyelitis Cases, January 1, 2010–June 1, 2010.

WPV1 and WPV3 denote cases of wild-type poliovirus types 1 and 3, respectively. The total number of cases is 254. Data are from the WHO Global Poliomyelitis Eradication Initiative.

the location of recent cVDPV outbreaks), isolated paralysis cases attributed to cVDPV have occurred in both normal and immunodeficient persons, and cVDPVs unassociated with disease have been detected with environmental sampling.³

Most cVDPV outbreaks have been controlled relatively easily with focused supplemental immunization campaigns. The extensive type 2 cVDPV epidemic that began in Nigeria in 2006 — the subject of the report by Jenkins and colleagues in this issue of the *Journal* (pages 2360–2369) — is an exception. Multiple independent cVDPV lineages developed over several years, enabled by low tOPV-immunization rates and an emphasis on con-

trolling wild-type infection with type 1 and type 3 monovalent vaccines. The epidemic proved extremely difficult to control with tOPV. Fortunately, only a handful of type 2 cVDPV cases have been observed since the first half of 2009, but Jenkins and colleagues verify that cVDPVs can be as infectious and virulent as WPVs.

The emergence of cVDPVs forces us to accept the reality that we are fighting fire with fire and that once eradication of WPV is assured, the use of live poliovirus vaccines will need to cease globally in a coordinated manner. Because cVDPVs will probably continue to circulate for at least 1 to 3 years after WPVs are eradicated,⁴ and live polioviruses may be reintroduced from rare

immunodeficient persons who continue to excrete virus,⁵ the world will need to rely on inactivated poliovirus vaccine (IPV) indefinitely to maintain immunity. Most economically advanced countries now use IPV exclusively. Infants and young children in developing countries can be provided with excellent protection if given two or more IPV doses, but as compared with OPV, IPV provides less protection to unimmunized persons through herd immunity; it also requires an injection and costs more than OPV to manufacture. Antigen-sparing techniques such as intradermal administration could reduce IPV costs significantly, making it more affordable for low-income countries that will probably bear

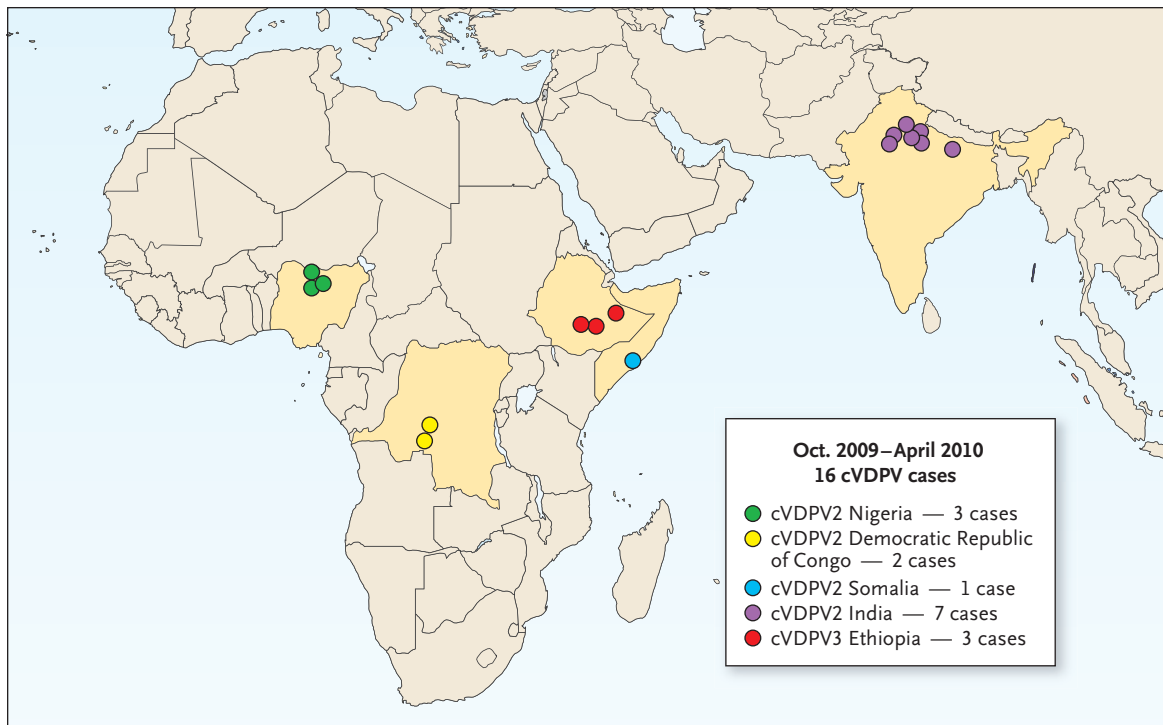


Figure 2. Current Outbreaks of Circulating Vaccine-Derived Poliomyelitis.

The abbreviation cVDPV denotes circulating vaccine-derived poliovirus, and cVDPV2 and cVDPV3 denote types 1 and 3, respectively. Data are from the WHO Global Poliomyelitis Eradication Initiative.

the burden of cVDPV outbreaks in a post-eradication environment.

The study reported on by Mohammed and colleagues in this issue of the *Journal* (pages 2351–2359) compared the effectiveness of intradermal injection of one fifth the standard dose of IPV in infants 2, 4, and 6 months of age using an investigational needlefree device with the effectiveness of intramuscular administration of the standard IPV doses for poliovirus types 1, 2, and 3. Intradermal administration of the fractional dose induced seroconversion to each serotype in more than 95% of subjects, which compared well with the conversion rate associated with intramuscular injection

of the standard dose. Ultimately, intradermal injection of a smaller dose must be compared with other strategies designed to reduce the cost of IPV, such as reduction in the number of doses administered, use of adjuvants, combination with other routine infant vaccines, and development of more immunogenic vaccines.

In any case, however, the health ministers in developing countries will have little interest in adopting IPV until global eradication of WPV is in sight and large cVDPV outbreaks are under control. Meanwhile, the Global Poliomyelitis Eradication Initiative (GPEI) of the World Health Organization (WHO) and its partners face many challeng-

es. Virulent polioviruses continue to cause paralytic disease in approximately 15 countries in Africa and Asia. Critics challenge the feasibility of eradication and the wisdom of devoting hundreds of millions of dollars to a single disease, arguing for a more integrated approach to control of serious global health problems. Funding of the program, which has spent more than \$8 billion over the past two decades, is precarious, and donors are signaling that their patience is limited.

But there are reasons for hope. Widened use of monovalent and bivalent type 1 and 3 OPV formulations that are more immunogenic than tOPV markedly reduced wild-type disease in Nigeria and

India in 2009; only two cases of wild-type poliomyelitis have been reported in India since early February 2010. Overall, according to the WHO, about half as many cases of wild-type polio have been reported globally in 2010 as during the same period last year. The Bill and Melinda Gates Foundation has entered the fray, contributing \$700 million, and Mr. Gates traveled to Nigeria in 2009 to meet with governmental and religious leaders to support the eradication program. The GPEI

team has developed a new strategic plan designed to align polio eradication with other global health priorities and continues to apply new insights from laboratory advances, epidemiologic studies, and disease modeling. This team's extraordinary dedication and determination to succeed should not be underestimated.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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