The Demise and Rebirth of Polio—A Modern Phoenix?

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(See the article by Estivariz et al., on pages 347–54.)

In 1991, one of us wrote in a commentary that “The eradication of polio by the year 2000 would be a magnificent gift from the 20th century to future generations of children” [1]. That remains no less true today. However, although the burden of polio has been dramatically lowered by the intense effort to enact its ultimate demise, the goal of eradication has not yet been achieved. The polio-eradication effort is led by a dedicated team at the World Health Organization that has repeatedly examined the reasons for the delay in achieving the eradication goal and modified its operational strategies—although the primary tool remains repeated mass immunization with live Sabin strain oral poliovirus vaccines. While there are difficulties for vaccination in areas of strife, religious and political barriers to immunization, and communities with tremendous population densities and poor hygiene, it is still anticipated that these can be overcome by tenacious efforts at repeatedly vaccinating every child.

Perhaps least expected—and in some ways the most difficult to deal with—are a small but growing number of “experiments in nature” in which Sabin polio strains circulate silently for several years and ultimately undergo sufficient mutational changes to cause outbreaks of paralytic disease that are clinically and epidemiologically indistinguishable from naturally occurring wild-type polio disease [2, 3].

The settings in which these circulating vaccine-derived polioviruses (cVDPVs) emerge seem fairly stereotyped. They usually occur in highly dense populations with low oral polio vaccine (OPV) coverage. cVDPVs have occurred with all 3 polio strains, and all have demonstrated both mutational change and frequent genomic recombination with other group C enteroviruses. A surprising number have occurred on islands. In settings with better hygiene and higher immunization rates (e.g., Cuba and New Zealand), OPV appears to be highly unlikely to continue to circulate [4, 5]. The first reported cVDPV outbreak occurred on the island of Hispaniola in 2000. [6] One striking paralytic case was discovered in a remote village in Haiti that was accessible only by foot. The extent of spread was demonstrated by environmental sampling in which 7 of the 10 polio isolates were cVDPVs from geographically distinct areas of the island [7].

The concept of a molecular clock that enables a reasonably accurate description of the time that has passed since the Sabin strain was first delivered as a vaccine dose based on the degree of sequence divergence in the VPI capsid region is key to our understanding of the evolution of cVDPV [3]. These clocks have commonly shown that cVDPVs have silently circulated for several years before their recognition—a very concerning observation with regard to declaring polio eradication or discussing cessation of immunization.

In this article of the Journal, Estivariz et al. [8] report the largest cVDPV outbreak to date, from the island of Madura in Indonesia—45 confirmed cases and another 10 cases of acute paralytic disease most likely to have been caused by cVDPV. It occurred at a time when wild-type polio had been imported onto the island of Madura as part of a wave of polio that spread across the Muslim world after the cessation of immunization in northern Nigeria. The observation that the paralytic disease attack rates were comparable for cVDPV and wild-type polio in the same population is added confirmation that cVDPVs are often fully virulent polioviruses in nature, as they are in the laboratory and in animal models.

There was evidence of 4 lineages of cVDPV type 1 on Madura, circulation was judged to have occurred for up to ~2 years before recognition, and cases occurred all over the island (although they were concentrated in pockets of low immunity among young children). The 4 lineages suggest even more strongly that continued circulation and evolution of Sabin strains will occur in parts of the de-
veloping world and that the harder we look the more that will be found. Most cVDPV outbreaks to date have been readily interrupted by mass campaigns employing OPV, including the more effective monovalent OPV vaccines, although a recently reported type 2 cVDPV outbreak in northern Nigeria is proving more difficult to control because of the lack of a public health infrastructure and other challenging conditions present in this region [9].

We now understand that we will face the near certainty of pathogenic cVDPV outbreaks as we attempt to eradicate naturally occurring wild-type poliovirus transmission and at least for the first few years after global cessation of routine OPV [10]. Urgency exists to develop coherent and effective vaccine strategies for managing cVDPV because of universal concern that, as wild-type polio is finally controlled, the impetus for continued high immunization coverage and the successes of supplemental immunization activities will wane. At the same time, the response options become more complex because of the reluctance to reintroduce OPV viruses back into the environment. What else can be done to aid these final steps in polio eradication? There is a growing consensus that inactivated poliovirus vaccine (IPV) may contribute to more rapid eradication of wild-type polio and control of emergent cVDPV when used in conjunction with existing OPV strategies. We need to set up pilot projects that enable us to look at what happens to Sabin virus circulation when IPV is substituted for OPV and to determine whether cVDPV outbreaks can be controlled with IPV. We also need to carefully examine the increasing number of cVDPV isolates for clues to the mutations that change attenuation and transmissibility. We need to examine host and societal factors that allow continued circulation of OPV. Other questions of concern include the following: Are there more subtle host factors that impair the immune response to vaccine and/or the ability to terminate viral shedding than the recognized risk with B cell deficiencies? Why is the antibody response to OPV in the developing world so much poorer than in the industrial world? What happens if you study in detail a group that has not responded to the standard 3 doses of vaccine with a subsequent dose of vaccine?

All of these questions seem to pose daunting tasks in the face of the daily battle to control polio, but understanding these factors may be equally important to the ultimate goal of polio eradication as the next successful mass campaign or new operational strategy. The phoenix has already lived longer than we predicted. Its offspring must not be permitted to rise from the ashes.

References