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Eradication of Poliovirus: Fighting Fire With Fire

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Eradication of Poliovirus: Fighting Fire With Fire

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(See the article by Wassilak et al., on pages 898–909.)

Endemic wild polioviruses have been eliminated from most of the world, and the number of human paralytic cases has been reduced by >99%, from an estimated annual incidence of >500,000 cases to <2,000 cases [1–3]. Circulating wild polioviruses remain endemic in only 2 major locations, Nigeria and a zone extending from northern India west to Pakistan and Afghanistan [1–3]. Furthermore, wild-type 2 poliovirus has been eliminated altogether, with the last documented case reported in northern India in 1999 [4]. These remarkable accomplishments represent a triumph for oral poliovirus vaccine (OPV), composed of attenuated variants of the 3 poliovirus serotypes [5]. OPV is administered by mouth, induces mucosal and humoral immunity, and is relatively inexpensive to produce—attributes that have contributed to its widespread use even in regions with rudimentary health systems.

However, OPV has an Achilles heel. The attenuated variants in the vaccine are rapidly replaced by revertant mutants, even on a single passage through the human intestine [6]. The revertant genotype has been mapped to a limited number of point mutations [7, 8], and revertant viruses can be distinguished genetically from wild polioviruses [8]. OPV vaccinees excrete a mix of viruses, some of which are as paralytogenic as wild polioviruses. These excreted viruses, similar to wild polioviruses, are readily transmitted to contacts of vaccinated infants and children by the fecal-oral route. Therefore, after mass OPV vaccination campaigns, the environment is inundated with a mix of excreted viruses, some of which have the disease potential of wild polioviruses. Therefore, the use of OPV could be considered to be an example of fighting fire with fire.

The dangers of OPV were recognized during early vaccine trials, and one epidemiologist coined the epigram “in like a lamb out like a lion” [9 p. 1214]. On the basis of meticulous surveillance in the United States, vaccine-associated paralytic poliomyelitis was documented both in vaccinees and their immediate contacts [10–14]. However, vaccine-associated paralytic poliomyelitis in contacts was rare and sporadic, occurring at a rate of 1–2 cases per 1,000,000 primary vaccinations. In retrospect, it is likely that vaccine-derived polioviruses (VDPV) did not spread widely in the United States because most susceptible children were vaccinated with OPV, rendering them resistant to virus shed by their vaccinated contacts.

Since 2000, >15 outbreaks of paralytic poliomyelitis caused by circulating VDPV (cVDPV) have been recognized throughout the world [1]. Such outbreaks have shared one epidemiological characteristic. They have occurred in areas where OPV vaccination coverage has been incomplete; thus, >50% of children remained susceptible. Under these circumstances, cVDPV can circulate for many generations, infect large numbers of persons, and cause outbreaks of paralytic poliomyelitis.

The article by Wassilak et al [15] in this issue of the Journal and a companion article [16] describe the most significant of these outbreaks of cVDPV. The Nigerian epidemic, in which type 2 VDPV has caused >300 paralytic cases, began in 2005 and has continued through 2010. Because wild-type 2 poliovirus causes only 1 paralytic case per 2000 infections [1], the Nigerian outbreak might represent >600,000 infections with virulent VDPV.

Under what circumstances did this outbreak occur? First, similar to other outbreaks of cVDPV, the epidemic was concentrated in the northern region of Nigeria, where there were relatively low rates of OPV vaccination [15]. Second, during 2006–2010, most of the vaccination campaigns in Nigeria used either monovalent or, more recently, bivalent vaccine lacking type 2 OPV. The
decision to use these formulations was based on an attempt to control wild-type 1 and 3 polioviruses at a time when wild-type 2 had been eliminated. Monovalent and bivalent formulations that omit type 2 OPV are much more effective than is trivalent OPV [17, 18]. In 2009, the dramatic increase in cases due to type 2 cVDPV led to several rounds of trivalent OPV, which may account for the rapid decrease in the number of type 2 cases in 2010. However, this outbreak has not yet been terminated, posing the potential threat of re-introduction of virulent type 2 polioviruses. Because wild-type 1 and 3 polioviruses frequently spread from Nigeria to neighboring countries in Africa, this constitutes a significant contingency [19].

The occurrence of repeated outbreaks of cVDPV and the magnitude of the Nigerian epidemic have sent a clear message. True eradication can only be achieved with the elimination of all circulating polioviruses. In countries or continents where wild polioviruses have been eliminated, there should be a transition from OPV to inactivated poliovirus vaccine. Many industrialized countries have already made this shift, which occurred in the United States during 1998–2000 [14]. Although there is no universal consensus, a number of experts have advocated this strategy [20–27]. Because inactivated poliovirus vaccine is expensive to manufacture and must be injected, this approach is costly. Several donors (including Rotary International and the Bill and Melinda Gates Foundation) have made significant commitments to underwrite this campaign for low-income countries.

Although recent history compels caution, it appears that the world may be on the cusp of elimination of indigenous wild polioviruses. When this goal is achieved, it will then be necessary to terminate the use of OPV if true eradication of circulating polioviruses is to be accomplished.

References


