4-1-2011

Eradication of Poliovirus: Fighting Fire With Fire

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(See the article by Wasssilak 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 <2000 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

Received 15 November 2010; accepted 16 November 2010.

Potential conflicts of interest: none reported.

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The Journal of Infectious Diseases 2011;203:889–90

1537-6613/2011/2037-0001$15.00
DOI: 10.1093/infdis/jiq148

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

1. Centers for Disease Control, Prevention. Progress toward interruption of wild poliovirus transmission worldwide, 2009. MMWR Morb Mortal Wkly Rep **2010**; 59:545–50.
2. World Health Organization. Progress towards interruption of wild poliovirus transmission worldwide, 2009. Wkly Epidemiol Rec **2010**; 85:178–84.
3. Nathanson N, Kew OM. From emergence to eradication: the epidemiology of poliomyelitis deconstructed. Am J Epidemiol **2010.** DOI: 10.1093/aje/kwq320.
4. Centers for Disease Control, Prevention. Apparent global interruption of wild poliovirus type 2 transmission. MMWR Morb Mortal Wkly Rep **2001**; 50:222–4.
5. Sabin AB. Present position of immunization against poliomyelitis with live virus vaccines. Br Med J **1959**; 1:663–80.
6. Evans DMA, Dunn G, Minor PD, et al. Increased neurovirulence associated with a single nucleotide change in a noncoding region of the Sabin type 3 poliovaccine genome. Nature **1983**; 314:548–50.
7. Minor PD. The molecular biology of poliovaccines. J Gen Virol **1992**; 73: 3065–77.
8. Kew OM, Sutter RW, de Gourville EM, et al. Vaccine-derived polioviruses and the endgame strategy for global polio eradication. Annu Rev Microbiol **2005**; 59:587–635.
9. Dick G. Immunity to poliomyelitis. Br Med J **1963**; 2:1468–9.
10. Henderson DA, Witte JJ, Morris L, et al. Paralytic disease associated with oral polio vaccines. JAMA **1964**; 190:41–8.
11. Schonberger LB, McGowan JE Jr, Gregg MB. Vaccine-associated poliomyelitis in the United States, 1961-1972. Am J Epidemiol **1976**; 104:202–11.
12. Nkowane BM, Wassilak SGF, Orenstein WA, et al. Vaccine-associated paralytic poliomyelitis, U.S.A. 1973-1984. JAMA **1987**; 257:1335–40.
13. Strebel PM, Sutter RW, Cochi SL, et al. Epidemiology of poliomyelitis in the United States one decade after the last reported case of indigenous wild virus-associated disease. Clin Infect Dis **1992**; 14:568–79.
14. Alexander LN, Seward JF, Santibanez TA, et al. Vaccine policy changes and epidemiology of poliomyelitis in the United States. JAMA **2004**; 292:1696–701.
15. Wassilak W, Ali Pate M, Wannemuehler K, et al. Outbreak of type 2 vaccine-derived poliovirus in Nigeria: emergence and widespread circulation in a underimmunized population. J Infect Dis **2010.** DOI:10.1093/infdis/JIQ140.
16. Jenkins HE, Aylward RB, Gasasira A, et al. Implications of a circulating vaccine-derived poliovirus in Nigeria. N Engl J Med **2010**; 362:2360–9.
17. Jenkins HE, Aylward RB, Gasasira A, et al. Effectiveness of immunization against paralytic poliomyelitis in Nigeria. N Engl J Med **2008**; 359:1666–74.
18. Sutter RW, John TJ, Jain H, et al. Immunogenicity of bivalent types 1 and 3 oral poliovirus vaccine: a randomised, double-blind, controlled trial. Lancet **2010.** DOI:10.1016/s0140-6736(10)61230-5.
19. http://www.who.int/csr/don/2010_11_09/en/, Accessed 13 November 2010.
20. Fine PE, Oblapenko G, Sutter RW. Polio control after certification: major issues outstanding. Bull World Health Organ **2004**; 82:47–52.
21. Sutter RW, Cáceres VM, Más Lago P. The role of routine polio immunization in the post-certification era. Bull World Health Organ **2004**; 82:31–9.
22. Agol VI. Vaccine-derived polioviruses. Biologicals **2006**; 34:103–8.
23. Dowdle W, van der Avoort HG, de Gourville E, et al. Containment of polioviruses after eradication and OPV cessation: characterizing risks to improve management. Risk Anal **2006**; 26:1449–69.
24. Heymann DL, Sutter RW, Aylward RB. A vision of a world without polio: the OPV cessation strategy. Biologicals **2006**; 34:75–9.
25. Chumakov K, Ehrenfeld E, Wimmer E, et al. Vaccination against polio should not be stopped. Nat Rev Microbiol **2007**; 5:952–8.
26. Ehrenfeld E, Glass RI, Agol VI, et al. Immunisation against poliomyelitis: moving forward. Lancet **2008**; 371:1385–7.
27. Thompson KM, Tebbens RJ, Pallansch MA, et al. The risks, costs, and benefits of possible future global policies for managing polioviruses. Am J Public Health **2008**; 98:1322–30.