The Polio Eradication Effort: Should Vaccine Eradication Be Next?

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Eradication of smallpox ranks as one of medical science's greatest contributions to public health, saving millions from disease and eliminating the need for vaccination. The World Health Organization (WHO), in cooperation with the Centers for Disease Control and Prevention (CDC), Rotary International, and governments around the world, is in the process of completing another such accomplishment, but in a considerably different social climate and with a different pathogen. The worldwide effort to eradicate polio is likely to reach its goal by 2003, if current levels of funding and cooperation continue. While we applaud this goal and the progress that has been made, we feel that the crucial final steps in the campaign need to be reconsidered.

The WHO has implemented a plan that takes advantage of the seasonal nature of poliovirus spread. National Immunization Days (NIDs) are held during the winter, or "polio-low season." They involve massive publicity campaigns, followed by door-to-door visits to unvaccinated households. Additional doses of the vaccine are distributed as needed during the "high season," when outbreaks occur. This approach maximizes the effect of vaccination and bypasses many of the logistical difficulties of a year-round effort. The eradication campaign uses live Sabin oral polio vaccine (OPV) exclusively, because it is cheaper than inactivated polio vaccine (IPV) and does not require trained personnel and sterile needles (*1*), resources which many lesser developed countries lack.

The WHO also rigorously tracks cases of infantile paralysis and screens sewage and river water for poliovirus in targeted areas. Whenever an outbreak is detected, a local immunization campaign is carried out to prevent the virus' spread (*2*). The results of the eradication effort have been impressive. Poliomyelitis caused by wild-type poliovirus (wild polio) is rapidly vanishing from even the most remote regions worldwide. The CDC projects that the world will be polio-free by 2003 (*3*), leaving behind a medical infrastructure for vaccination that can then be used in a campaign against measles. Under this plan, polio vaccination will be stopped by 2005, which will save about $200 million a year in vaccine-associated expenses in the U.S. alone (*3*). After this date, laboratory stocks of poliovirus would either be destroyed or restricted to high-level containment facilities (*3*).

While this plan is promising, it is not complete. Because the WHO is relying on OPV, certification of an area as "polio-free" is accurate only by a narrow definition: no wild polio detectable in the population, the sewage, or the drinking water over a period of years. Because Sabin strains mutate readily back to virulent forms (*4*), potentially pathogenic viruses are still being released into the aquifers. Vaccine-associated poliomyelitis will still occur in these "polio-free" areas, at rates of 1 in 300,000 (*5*) to 1 in 500,000 (*6*) recipients of OPV. Because recycling of waste water is necessary in many parts of the world, virus excreted by vaccinees may persist indefinitely (*7*).

A broader, more intuitive definition of eradication would be elimination of both vaccine and wild strains—a goal that cannot occur if only OPV is used. Difficulties in distribution and lack of medical resources are cited as reasons for using OPV, but terminating the effort without making a transition to IPV contradicts the WHO goal of establishing an infrastructure for future eradication campaigns. One way to accomplish both goals would be to continue polio vaccination until IPV can be distributed worldwide. Then the campaign would not be an isolated effort, but part of a broader public health initiative (*8*).

Before vaccination can be stopped safely, it will be necessary to destroy most existing viral stocks and restrict access to the remainder to prevent accidental and deliberate release. For smallpox, virus stocks were located in only a few institutions before eradication, which meant that inventory control was relatively straightforward. There is no central record of poliovirus stocks, which are distributed among hundreds, or possibly thousands, of sites. Without an accurate inventory, it is unlikely that all virus stocks can be found and destroyed. For example, during structural studies of coxsackievirus B1, an enterovirus, it was discovered that the virus stock was contaminated with polio (*9*). This incident emphasizes the difficulty in identifying poliovirus repositories in research laboratories. Experience with influenza virus suggests that accidental release of an infectious agent from laboratory stocks may occur (*10*). As with smallpox, there is the possibility that some wild virus will survive for long periods in the environment (*11, 12*). Even if total virus destruction could be accomplished, the small size of the poliovirus genome (7.5 kb), whose sequence is known (*13, 14*) and whose complementary DNA is infectious (*15*), would make it possible for a terrorist to synthesize a new stock.

In the post-vaccine world, the susceptible population would increase each year and the large number of potential sources of reintroduction would soon constitute a major threat. Vaccination of laboratory personnel who are studying the virus or maintaining emergency vaccine stocks then creates a dilemma. If workers are vaccinated with OPV, they will shed live poliovirus into the environment. Use of IPV would allow these workers to act as carriers (because infection of the gut is still possible), increasing the probability of an outbreak. For smallpox, the fact that vaccine and virulent strains differ substantially made it possible to avoid this difficulty.

To evaluate the potential impact of a single reintroduction of poliovirus into the post-vaccine world, we can use the 1992–93 Dutch epidemic as a model. In this incident, 67 cases of paralytic poliomyelitis were reported, but the virus spread to many more individuals. High levels of vaccination with IPV meant that the paralytic cases were restricted almost entirely to members of a religious group that refused the vaccine (*16*). Within this subpopulation and its immediate contacts, the virus spread very efficiently; ~7% of the children in this group were actively secreting wild polio in a single sampling taken during the epidemic (*17*). This epidemic occurred in a nation with high standards of health care, where paralytic cases were reported promptly and additional doses of IPV and OPV were distributed to the affected area immediately. Such high standards of preparedness are unlikely to continue after cessation of vaccination. In a city of 10 million unvaccinated individuals, a rough estimate would be that a single release of virus could result in 7000 paralytic cases. It would take more than 700 years of vaccination to produce that number of cases of vaccine-associated paralysis in the U.S.

The control of poliomyelitis has substantially improved the quality of life worldwide, and the completion of this task will allow lesser developed countries to focus on other public health issues. To succeed, however, the polio eradication effort should take a balanced approach as part of a larger campaign to improve health and sanitation.

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Ending Polio Immunization

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The financial, logistical, and biological challenges of eradicating polio were recognized long before the goal of global polio eradication by the year 2000 was set in 1988 (*1*, *2*). During planning for the initiative, it was recognized, though, that answers to some issues would become apparent only as the initiative matured. Nine years later, the strategies have been clearly defined (*3*), and rapid progress is being made. Only 4000 polio cases were reported worldwide in 1996, which is a decline of nearly 90% from the 35,000 cases reported in 1988. Polio eradication in the Western Hemisphere was certified in 1994, and wild-type poliovirus (wild polio) circulation is now largely confined to South Asia and Africa (*4*). The initiative is entering a new phase. In addition to interrupting final chains of transmission, the initiative must now address concerns about what will happen after wild polio is eradicated.

Eventual cessation of control measures is inherent to the concept of disease eradication; it has always been anticipated that immunization against poliomyelitis would be stopped. Potential strategies for stopping immunization were reviewed at meetings of the World Health Organization (WHO) Technical Consultative Group held in 1996 and 1997. The WHO's Plan of Action for Global Polio Eradication calls for a specific strategy for cessation of immunization to be developed even before the world is certified as free of polio.

Dove and Racaniello question whether it will ever be possible to stop polio immunization (*5*). They cite three specific concerns: possible persistence of wild polio in the environment, potential for wild polio to escape from laboratories, and potential for continued circulation of vaccine viruses after use of the oral polio vaccine (OPV) is halted. In a review of potential environmental reservoirs of wild polio (*6*), Dowdle and Birmingham state, "The rate of poliovirus inactivation is dependent on numerous conditions, but survival in the environment is finite," with survival in the environment lasting months rather than years. They conclude that the only environmental source that presents a serious threat to the eradication initiative is laboratory stocks of wild polioviruses. An escape of a wild polio strain through a laboratory accident has recently been documented in the Netherlands (*7*).

Dove and Racaniello imply that inventory, control, and containment of all clinical materials, extracts, poliovirus isolates, and other potentially infectious materials are unmanageable tasks. However, the magnitude of these tasks and the international cooperation needed to achieve them pale when compared with tasks already accomplished (*4*, *8*, *9*). The formal process of containing wild polio stocks will begin with a consultation of vaccine manufacturers, technical organizations, and research institutions, which will be convened by the WHO in September 1997. The expected outcome of this meeting is a draft plan for containment procedures that will be widely circulated in the scientific community before implementation.

The potential for the Sabin strains to persist or revert to neurovirulence was debated even before the widespread introduction of the Sabin vaccine (*10*). Although some immunocompromised individuals have excreted vaccine strains for 2 years or more (*6*), there are no data to show that vaccine viruses persistently circulate in a general population or cause outbreaks of paralytic poliomyelitis. In 1961, Fox noted "the clearly limited ability of Sabin viruses to spread, as compared with that of the wild viruses . . ." in Louisiana (*11*). Data from Cuba (*12*) and Hungary (*13*), where OPV was given exclusively through mass campaigns, support Fox's findings. In these countries, Sabin viruses could be isolated from clinical and environmental specimens only in the months immediately after the campaigns.

However, given the importance of assessing this theoretical risk, the WHO is sponsoring studies to determine how and when immunization can be stopped. These include the prevalence and duration of excretion of vaccine virus in immunodeficient persons in both industrialized and developing countries (*14*). Nucleotide sequencing studies (*15*) of vaccine-derived virus isolates from paralyzed children in nonendemic developing countries are under way to estimate the interval between the administration of the original vaccine dose and collection of the stool sample.

Dove and Racaniello suggest that inactivated polio vaccine (IPV) should replace live OPV either on a permanent or an interim basis to guard against continuing circulation of the Sabin viruses after the eradication of wild viruses. Although the infrastructure exists to deliver IPV (*16*), such a decision cannot be made lightly. Operational IPV production capacity is quite limited and would have to be expanded for IPV to be used worldwide. Halting the use of OPV remains the simplest and most cost-efficient means for stopping immunization. This option should not be abandoned without compelling reasons to do so.

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