

EDITORIALS



Monovalent Oral Poliovirus Vaccines — A Good Tool but Not a Total Solution

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The polio eradication campaign initiated in 1988 by the World Health Organization (WHO) led to an impressive decline in cases of paralytic poliomyelitis around the world. The eradication strategy involved highly organized mass immunization campaigns, relying solely on the trivalent oral polio vaccine developed by Albert Sabin and licensed in the United States in 1963. Monovalent versions of oral polio vaccine had been licensed earlier but were abandoned in favor of the trivalent combination oral polio vaccine to simplify immunization schedules. Efficacy was not considered to be a significant issue, and differences between monovalent and trivalent vaccines were never formally assessed.

At the turn of the century, global transmission of wild-type poliovirus type 2, one of the three serotypes of the virus, had been successfully interrupted. The elimination of this serotype represented a milestone for the eradication initiative; however, further progress toward eradication began to falter. Even today, circulation of endemic virus continues in several geographic pockets (northern Nigeria, northern India, and the Pakistan–Afghanistan border) that continue to be a source of reintroduction of wild-type virus into countries where transmission had previously been stopped. Obstacles to eradication have included incomplete vaccination coverage and inadequate efficacy of oral poliovirus vaccine. In some densely populated areas of India, it appeared that trivalent oral poliovirus vaccine was not sufficiently immunogenic to eliminate the circulation of wild-type virus, especially in the context of extraordinarily high birth rates, poverty, and poor sanitation. New vaccine products were sought to achieve

the final goal of eradication. A few previous trials of monovalent oral poliovirus vaccine had suggested that monovalent type 1 oral poliovirus vaccine was two to three times as immunogenic as trivalent oral poliovirus vaccine¹ because it eliminated interference from the other two poliovirus serotypes. The Global Polio Eradication Initiative issued an urgent call for the development of a monovalent product to boost immunogenicity, and in 2005, a new monovalent type 1 oral poliovirus vaccine with higher potency was quickly licensed and put to use.

In this issue of the *Journal*, two clinical studies are reported that provide direct comparisons of the efficacies of the new monovalent type 1 oral poliovirus vaccine and the conventional trivalent oral poliovirus vaccine. One study² of vaccine-induced protection was conducted in northern Nigeria, where a temporary suspension of all poliovirus immunization in one state in 2003 contributed to a national epidemic of poliomyelitis and reinfection in more than 20 countries that had been poliomyelitis-free. Even after the reversal of the suspension, vaccine coverage has remained low in northern Nigeria. According to field studies of the reported number of doses received by case patients and matched controls, the estimated efficacy of monovalent type 1 oral poliovirus vaccine per dose against type 1 poliomyelitis was four times as great as that of the trivalent oral poliovirus vaccine. At the same time, a new strategy of vaccine delivery, in which oral poliovirus vaccine was offered together with a range of additional pediatric vaccinations and other health services, resulted in moderate gains in coverage. Together, these two interventions

markedly increased vaccine-induced immunity in the region.

The other study, designed to directly measure immunogenicity, took place in Egypt.³ Seroconversion rates were determined after administration of a dose of either vaccine at birth, and virus excretion was measured after subsequent challenge with monovalent type 1 oral poliovirus vaccine. The results showed that when given at birth, monovalent type 1 oral poliovirus vaccine was more effective at inducing production of humoral antibodies and at reducing virus excretion after challenge. The relative contributions of increased vaccine potency and lack of interference by the other two serotypes to the increase in efficacy is not known.

Both of these studies confirm the potential usefulness of supplemental doses of monovalent oral poliovirus vaccine as an effective tool for interrupting persistent chains of wild-type virus transmission, as previously shown in northern India,⁴ and thereby accelerating the path to eradication. The authors of the Nigerian study emphasize that in some regions, considerable improvements in vaccine coverage will still be required to eliminate the current gaps in immunity that impede eradication, despite the boost provided by monovalent oral poliovirus vaccine supplements. Although reducing vaccine failure does not compensate for failure to vaccinate, the newly formulated monovalent type 1 oral poliovirus vaccine and, by extrapolation, monovalent type 3 oral poliovirus vaccine are welcome additions to the toolbox we are relying on to eliminate transmission of wild-type polioviruses.

The damper on the fire of enthusiasm, however, is the growing realization that complete eradication of poliomyelitis must include eventual eradication of the live oral poliovirus vaccine itself, whether trivalent or monovalent.⁵ Documentation of the genetic instability of the oral poliovirus vaccine, emergence of circulating neurovirulent vaccine-derived polioviruses, long-term excretion of virus by immunodeficient vaccinees, and promiscuous recombination between vaccine polioviruses and nonpoliovirus enteroviruses have all been presented and discussed in the recent literature.⁶ Use of oral poliovirus vaccine must eventually stop; this step has been part of the eradication plan from the beginning. Unfortunately, poliovirus will not go away after circu-

lation of wild-type virus is halted, and a high level of immunity in the global population must be maintained — and not just in high-income countries that have already switched to the safer but more expensive inactivated poliovirus vaccine.⁷

Although accelerating the final steps to eradication of wild-type virus is unquestionably desirable, we must be prepared for the posteradication phase with a safe, affordable inactivated poliovirus vaccine that can be incorporated into a universal, routine pediatric immunization program. Inactivated poliovirus vaccine could also play a role in facilitating interruption of the transmission of wild-type virus in developing countries. Inclusion of an additional group in the Egyptian study might have been used to assess the effectiveness of inactivated poliovirus vaccine as a tool for interrupting virus transmission; preliminary studies conducted last year in Cuba showed that inactivated poliovirus vaccine effectively reduced transmission of the virus after an oral poliovirus vaccine challenge in that setting.⁸ Such data would help prepare for the ultimate and long-term incorporation of an inactivated poliovirus vaccine into the WHO Expanded Program on Immunization.

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