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Polio eradication: the endgame

In 1988 the World Health Organization (WHO) launched a global campaign to eradicate polio, the goal being eradication by 2000 and certification (absence of wild-type virus for at least 3 years) by 2005. Although short of this goal, results so far have been impressive: by 2000, paralytic polio cases decreased by 95% from an estimated 350,000 cases in 1988, and the number of endemic countries was reduced from 125 to 30. But eradication of the wild-type virus will not necessarily signify the end of the polio story. A recent polio outbreak in the Dominican Republic and Haiti may well push the agencies leading the campaign to reconsider their post-eradication strategy, and raises concerns over whether stopping vaccination will be at all possible.

Poliovirus is primarily an enteric virus that on rare occasion (<1% of infections) invades the central nervous system to cause paralytic complications and even death. In the 1950's two highly effective vaccines were developed: an attenuated live virus vaccine delivered orally (Sabin or OPV) and an inactivated virus vaccine delivered by injection (Salk or IPV). Both vaccines have been widely and successfully used to the extent that the Americas have been certified wild-type poliovirus-free since 1994. The WHO chose the OPV vaccine for the global eradication campaign because it is easier to administer, cheaper to produce and provides longer-lasting protective immunity. But always present was the inherent danger that the attenuated strain could revert to virulence, which is exactly what happened in the latest outbreak in the Caribbean. Nineteen cases were confirmed by laboratory analysis to be caused by a vaccine-derived revertant virus. Sequence analysis showed it had 97% homology with the OPV strain (normally vaccine-derived isolates are 99.5% similar to the parental strain). In comparison, wild-type polioviruses have 82% genetic identity to OPV. It is well known that OPV vaccine-derived viruses can revert and lead to paralytic polio but this occurs extremely rarely (1 in 2.4 million doses). The peculiarity of the Caribbean outbreak is that it came as a cluster of cases infected with a virus that may have circulated for 2 years in the population.

Will these events impact upon the overall eradication strategy? "Probably not" is the collective answer from WHO and CDC campaign coordinators, but some reassessment is inevitable. Increased surveillance and a comprehensive evaluation of the Caribbean outbreak are to be implemented, including the systematic sequence analysis of all poliovirus isolates worldwide. It is hoped that these analyses will give insights into crucial aspects of poliovirus natural history such as transmissibility and persistence in the environment.

The Caribbean incident is actually the third polio outbreak known to stem from a vaccine-derived virus. Retrospective studies have demonstrated that revertant strains were responsible for outbreaks in China and Egypt (see *News* page 135).

By definition, the ultimate goal of an eradication campaign is to discontinue control measures and to reap the social and financial benefits (estimated to be $1.5 billion/year after cessation of poliovirus vaccination). The ideal stratagem would be to simply phase out OPV vaccinations in a globally coordinated manner. However, the Caribbean and previous outbreaks illustrate that the risk of disease due to revertant virus is real and alternative strategies must be considered.

Continued immunization programs using the OPV strain would seem too risky, since the hazard of revertant viruses would remain. Vigilance to maintain high levels of immunization may be crucial during the later phases of the campaign since all 19 Caribbean cases were either non- or poorly-immunized. But perennial vaccination would be increasingly difficult to implement, especially in poor countries once the primary motivation, the burden of disease, is eliminated. Moreover the ultimate goal of halting vaccination would remain obviously, and painfully, unfulfilled.

A transitional program that would switch to IPV, possibly as part of a combination vaccine strategy, seems the most seductive solution scientifically. IPV is now the adopted standard in many industrialized nations including the United States, the Netherlands and Finland, and since it is a killed virus, will not generate revertants. The cost of such a shift in a global campaign would be significant since IPV is more expensive to produce and administer, and there is currently no global-scale production capacity. Another possibility would be to sequentially remove each of the three strains that comprise the OPV vaccine and appraise the consequences along the way.

The entire cost of the global campaign has been estimated at $2.5 billion. While the latter phases of the campaign are proving the most expensive, a final transition phase before complete cessation of immunization would represent only a fraction of the total cost. But before any strategy is adopted, further research must provide us with answers to the questions unearthed by this latest outbreak in the Caribbean.