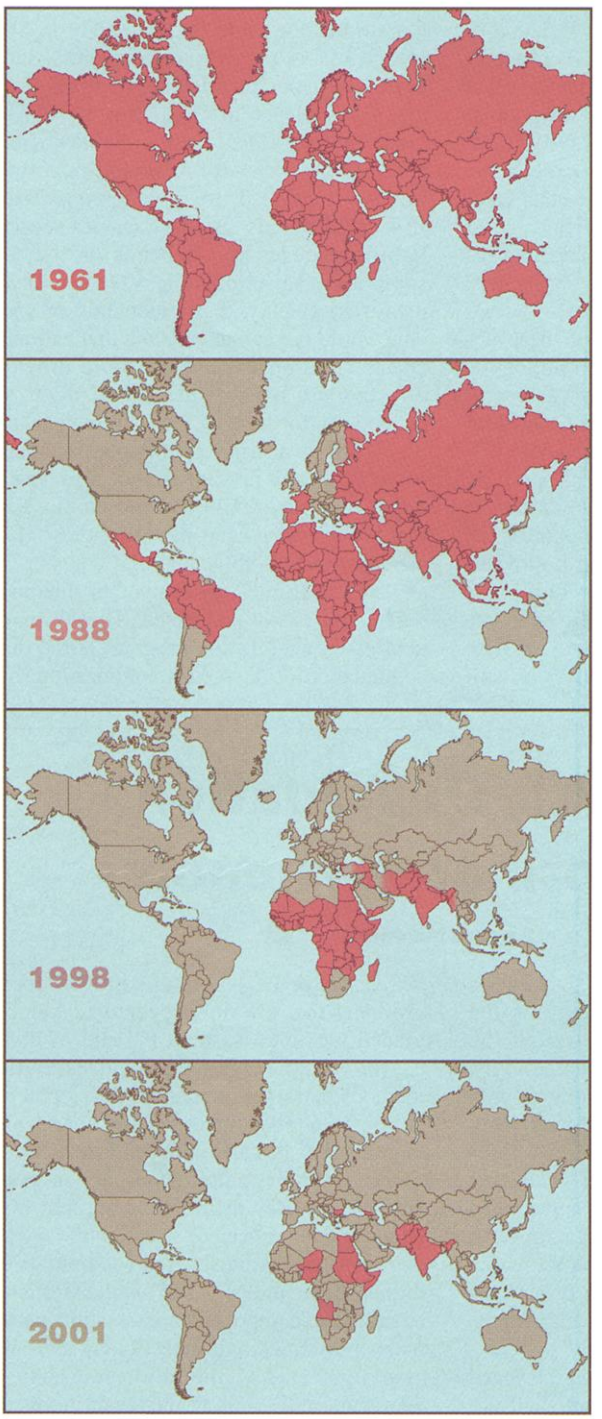
PERSPECTIVES: VIROLOGY

Poliomyelitis Eradication—a Dangerous Endgame

Neal Nathanson and Paul Fine

We are now poised to eradicate wild polioviruses from the world, a long-sought public health goal. At the close of 2001, wild polioviruses remained endemic in only 10 countries, and fewer than 1000 cases were recorded during that year. These numbers represent a marked improvement over the previous year, when almost 3000 cases were recorded in 20 countries; in 1988, the year that the global initiative for poliomyelitis elimination was launched, there were >350,000 cases worldwide (see the figure). The report on page 356 of this issue by Kew and colleagues (*1*) has important implications for current global efforts to eliminate poliomyelitis and for maintaining a polio-free world. These authors document an outbreak of paralytic polio on the island of Hispaniola (Haiti and the Dominican Republic) in 2000, the first report of poliomyelitis in this region in almost a decade.

Rapid progress in poliovirus eradication owes its success largely to the widespread use of the oral poliovirus vaccine (OPV) developed by Albert Sabin. Eradication of wild poliovirus is plausible because humans are the only hosts of human polioviruses, and because OPV has several major advantages. It is easily administered by mouth, which has facilitated the largest mass immunization campaign in history. OPV provides a long-lasting high level of mucosal immunity, thus reducing transmissibility of wild polioviruses. The live attenuated poliovirus in OPV spreads to some contacts of vaccinees, increasing the impact of the vaccine beyond those actually vaccinated. Finally, the elimination of wild polioviruses from much of the world is a testimony to the effectiveness of national and international public health programs. The progressive elimination of wild poliovirus began in 1963 in Cuba, the first country to implement a national immunization day (NID). This type of campaign led ultimately to the eradication of poliovirus from the Americas in 1991 and thereafter from European and Western Pacific regions (see the figure).



Worldwide elimination of wild poliovirus (1961–2001). Shown in red are countries with indigenous wild poliovirus in 1961, 1988, 1998, and 2001. Maps produced by the CDC after data from the World Health Organization.

Unfortunately, there is a problematic side to reliance on OPV. This vaccine contains three attenuated strains of poliovirus, one for each of the major immunotypes (types 1, 2, and 3). Each attenuated strain of virus was derived by classical methods of tissue culture passage and clonal selection for the attenuated phenotype. Detailed genetic analysis has revealed that the attenuation was due to a small number of critical point mutations (*2*). After ingestion, OPV replicates in the human intestine, with the generation of many mutants, some of which exhibit revertant phenotypes, which may resemble the neurovirulence of wild polioviruses. A high proportion of immunized subjects, perhaps 30% or more, excrete revertant strains of OPV, now called vaccine-derived polioviruses (VDPVs) (*3, 4*). VDPVs are highly enterotropic and spread readily to nonimmune subjects who come in contact with primary vaccinees.

At a population level, these characteristics have important implications. If close to 100% of a population is immunized, the vaccinees are exposed to the attenuated vaccine virus and develop immunity before revertant strains can cause paralysis. However, if immunization coverage is incomplete and a large proportion of the population does not participate, then a VDPV may spread sequentially through several nonimmunized persons, accumulating mutations and reversions, which will increase the likelihood that some individuals will develop paralytic poliomyelitis. In essence, a vaccine program might inadvertently initiate an outbreak of poliomyelitis, similar to natural outbreaks in the past. The circumstances favorable to such an occurrence, in particular low coverage and poor hygiene, have been reviewed and discussed extensively (*5–7*).

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SOURCE: OLEN KEW

The report by Kew *et al.* (*1*) provides a detailed documentation of just such an episode on the island of Hispaniola. The authors provide impressive evidence that a single type 1 OPV virus underwent reversion and recombination with a wild enterovirus, and then spread to cause more than 20 virus-confirmed cases of paralytic poliomyelitis. Because there are usually 100 to 250 infections per paralytic case, it can be inferred that this virulent virus infected several thousand individuals. Most of the cases were documented in unvaccinated or incompletely vaccinated children under 15 years of age, where only about 30% of the population had received three doses of OPV. Thus, the outbreak took place under exactly the conditions where it was postulated that OPV might spread (*5*). It is noteworthy that at least two other similar small outbreaks have been observed, in Egypt and the Philippines, under similar circumstances (*8, 9*).

What are the implications of these observations for the "endgame" in poliovirus eradication? Currently, in areas where wild poliovirus has been eradicated, children are still being immunized, either with OPV or with inactivated poliovirus vaccine (IPV, the Salk vaccine). Immunization is maintained to protect children against the possible reintroduction of wild poliovirus or exposure to VDPV. Once complete global eradication of wild poliovirus has been achieved and certified, there are several options. In regions where IPV is available, OPV could be discontinued, with the eventual discontinuation of IPV once monitoring provided the assurance that OPV and VDPV have disappeared from the world. IPV is much more costly to produce and more difficult to administer than OPV (*10*), so this option may not be feasible everywhere, at least in the near future.

In regions where IPV is not currently available, a massive final round of OPV could be administered, followed by careful monitoring for acute flaccid paralysis (the classic sign of paralytic poliomyelitis) supported by laboratory testing of fecal samples for evidence of circulating VDPV. In the event that VDPV were to be identified, it would be necessary to reintroduce routine vaccination or mass campaigns with IPV or OPV. This approach carries several liabilities because it depends on the assumptions that circulating VDPV will be identified quickly, that a stockpile of vaccine would be maintained, and that national and international agencies would provide effective assistance wherever it might be needed. Unfortunately, this strategy could be perceived as offering a double standard of public health prevention, because developing countries would be exposed to a risk that the industrialized nations—those that can afford IPV—could avoid.

The "endgame" poses another dilemma that is not easily addressed. The ultimate goal of the eradication program is the discontinuation of all polio immunization. Inevitably, an increasing number of people would become susceptible to these viruses. To ensure that poliovirus could not be introduced into a susceptible population, it would be necessary to destroy or contain all stocks of these viruses. This presents a challenge in that some fecal samples, collected for many different reasons and held in freezers worldwide, may be inadvertently contaminated with wild or vaccine-derived polioviruses. The World Health Organization is currently setting up a system to identify and minimize these risks, but the surveillance and contingency planning will have to extend long after successful eradication.

The endgame for poliovirus eradication offers challenges that would be daunting even for a chess master, let alone a world where global coordination of public health practice is an ideal yet to be realized.

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PERSPECTIVES: CHEMISTRY

Catalytic Degradation of Chlorinated Phenols

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Substances used in chemical synthesis may either be incorporated into the final product or pass through the process and emerge as waste. Increasingly, the chemical industry seeks products with high yield and low waste, allowing them to avoid paying first for material inputs and again for waste disposal. The concept of "atom economy" has been introduced to monitor the fate of the reactants. An atom-economic process is one in which the proportion of materials that is incorporated into the final product is maximized (*1, 2*).

For most chemical processes, however, the hypothetical zero-waste level will not be reached in the near future. Furthermore, products that are not recycled or biodegraded turn into waste at the end of their useful lifetime. New efficient catalytic methods therefore have to be developed to eliminate poorly biodegradable chemicals in industrial sites and in the environment.

For example, chlorinated phenols persist for decades in the environment because of their resistance to microbiological degradation, leading to the accumulation of these toxic molecules (*3*). Polychlorinated aromatic compounds are constituents of many pesticides and insecticides and are also generated in the chlorine-assisted degradation of lignin in the paper industry. Pentachlorophenol and 2,4,6-trichlorophenol (TCP) have been listed as priority pollutants by U.S. and European Environmental Protection Agencies.

These "recalcitrant molecules" are key targets for the evaluation of new catalytic oxidation systems that use metal complexes as catalysts. On page 326 of this issue, Sen Gupta *et al.* report a new oxidative cleaning method for chlorinated phenols, using hydrogen peroxide and iron catalysts (*4*). The metal center of these catalysts is chelated by tetraamido ligands called TAML, a family of macrocycles that has been developed by Collins and co-workers over the last two decades (*5*).

Nearly full conversions of pentachlorophenol or TCP are obtained at 25°C at pH 10 within a few minutes with a very low catalyst loading (0.05% with respect to the substrate to be converted). An excess of hydrogen peroxide (100 equivalents/TCP) was added by portions to limit its catalytic decomposition by the iron catalyst (Fe-TAML). The distribution of the degradation products of TCP (see the figure) indicates that 85% of the initial carbon atoms of the substrate are recovered in noncyclic products. Only 2% of the initial carbon atoms are still present as chlorinated aromatics after the catalytic oxidation of TCP, and no dioxin deriva-

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