

Two polio vaccines for defeating a paralysing scourge

Poliomyelitis is caused by an enterovirus that in rare cases invades the nervous system and damages motor neurons, causing permanent disability, paralysis or death. Today, the disease has been eradicated from all but a handful of countries, thanks to two types of polio vaccine developed in the 1950s: an injected vaccine containing inactivated virus, originally developed by researchers led by Jonas Salk, and an oral vaccine containing live attenuated virus, originally developed by Albert Sabin and colleagues.

Researchers had been attempting to develop a polio vaccine since the 1910s, but early efforts were either ineffective or too risky. A key milestone occurred in 1949, when Thomas Weller, John Enders, and Frederick Robbins demonstrated that poliovirus

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could be grown in the laboratory using skin and muscle tissues from human embryos (MILESTONE 9). This meant that the virus no longer needed to be grown in live monkeys, facilitating its production in the necessary quantities for vaccine testing and production. The three researchers shared the 1954 Nobel Prize in Physiology or Medicine.

Jonas Salk developed his inactivated polio vaccine by growing the virus in monkey kidney cells, then killing the virus with formalin. A placebo-controlled trial in 1954 involving 1.6 million children in Canada, Finland and the United States showed that the killed poliovirus vaccine was safe and effective at preventing infection with wild poliovirus. Between 1955, when Salk's vaccine went into widespread use in the United States, and 1962, it decreased the incidence of poliomyelitis by about 95%.

However, antibody levels in vaccinated individuals decreased within a few years, so whether the inactivated vaccine would provide permanent protection was unclear. In addition, poliovirus could still multiply harmlessly in the guts of vaccinated individuals, so it was thought that Salk's vaccine would not fully interrupt the circulation of wild poliovirus in the population.

Meanwhile, researchers learned in the 1940s that passaging poliovirus repeatedly through rodents and then through cell culture resulted in strains that were less virulent. These observations laid the groundwork for a live attenuated poliovirus

vaccine, but this was a complicated endeavour: a weakened strain had to be found that could not enter the nervous system but that could still multiply in gut tissues and trigger the production of antibodies. The weakened strain then had to be purified and produced in large quantities without regaining neurovirulence. Sabin's discovery that chimpanzees are the best animal model species to test gut infectivity of attenuated strains, while cynomolgous and rhesus monkeys are the best to test nervous system infectivity, helped guide these investigations.

Multiple researchers worked on the live attenuated polio vaccine effort throughout the 1950s, including groups led by Hilary Koprowski, Herald Cox and Sabin. By the time Sabin's strains were chosen as the safest in 1959, millions of doses of various experimental vaccines had been administered in studies around the world. The first nationwide mass vaccination campaign with Sabin's vaccine took place in Cuba in 1962, followed by other countries throughout the 1960s.

It soon became clear that the live vaccine occasionally caused poliomyelitis in vaccinated individuals, their contacts or members of the community. This occurred when random mutations accrued during replication of the vaccine virus in the intestine led to the regaining of neurovirulence. Thus, as countries brought wild poliovirus under good control, many switched to improved versions of the inactivated polio vaccine.

Countries where polio remains endemic continue to use the live oral polio vaccine because of its convenience and superior ability to induce mucosal immunity in the gut. Today polio continues to circulate in three countries: Afghanistan, Nigeria and Pakistan. Poor sanitation, lack of health-care infrastructure and opposition to vaccination campaigns by militant organizations have hampered the efforts to wipe out the virus for good.

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ORIGINAL ARTICLE Sabin, A. B. Immunization of chimpanzees and human beings with avirulent strains of poliomyelitis virus. *Ann. N. Y. Acad. Sci.* **61**, 1050–1056 (1955)

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