Scientists build a new vaccine arsenal to eradicate polio

June 14 2023

Credit: Unsplash/CC0 Public Domain

Despite some of the most successful international vaccination campaigns in history, the poliovirus continues to circulate around the world, posing a threat of neurological damage and even paralysis to anyone who is not

vaccinated.

While the original polio strains, called wildtype, have largely been eliminated, new strains can develop from the oral polio vaccine (OPV), which is the one most used in the developing world. Oral vaccines use live, weakened virus that occasionally mutates to an active form, leading to outbreaks even in countries believed to have eliminated polio.

Scientists at UCSF and the UK's National Institute of Biological Standards and Control (NIBSC) have developed two novel oral polio vaccines (nOPVs) to bolster the World Health Organization's most recent push to finally eradicate polio, which began two years ago using the first nOPV developed by the same team. These are the first new polio vaccines in 50 years.

Like the first nOPV, the two newest nOPVs, which were described in *Nature* on June 14, are made from weakened poliovirus that has been genetically engineered to reduce reversion to dangerous forms of the virus. The development of these new vaccines was led jointly by Raul Andino, Ph.D., UCSF professor of microbiology and immunology, and Andrew Macadam, Ph.D., a virologist at NIBSC.

"With such variation in vaccination within and between countries, poliovirus has persisted into the 21st century, with sometimes tragic consequences," said Andino, co-senior author of the paper along with Macadam. "We've designed these new vaccines using lessons learned from many years of fighting polio and believe they will help eliminate the disease once and for all."

The evolving battle against polio

Polio is insidious: it is usually asymptomatic, but can cause severe disability, paralysis or death in about one in every hundred children. It

spreads via fecal or oral particles, so it is particularly problematic in regions with poor sanitation. In the first half of the 20th century, polio outbreaks routinely rolled through the US, leading to a race to develop vaccines.

The first effective polio vaccines emerged in the 1950s, kicking off massive campaigns to immunize every person, with an emphasis on children. The inactivated polio vaccine (IPV), made of dead poliovirus, was given via injection, while the oral polio vaccine (OPV), made of weakened poliovirus, was given on a sugar cube or in a candy. Today, IPV is the vaccine of choice in countries with robust healthcare, and OPV—the cheaper, easier-to-administer option—is used otherwise.

In populations where everyone is immunized early in life, it doesn't matter whether they receive IPV or OPV, although these vaccines act in different ways in the environment. People vaccinated with IPV can still get infected with any polio that happens to be circulating. They will not get sick, but they can silently transmit the virus to the unvaccinated. People vaccinated with OPV can't silently transmit circulating polio in this way, but they can shed the weakened virus they were inoculated with and spread it to the unvaccinated. If the weakened virus mutates, it can become pathogenic polio once more.

In populations with unvaccinated children—whether due to refusal to vaccinate, natural disaster, or war—such vaccine-derived polio can spread widely, causing severe disease in the unlucky few.

While the original, or "wildtype," poliovirus has only been recently detected in Afghanistan and Pakistan, vaccine-derived polio has been detected in countries as far flung as Syria, the Democratic Republic of Congo, and the U.S. In fact, there have been more cases of vaccine-derived polio than wildtype in recent years, creating an urgency to counter this new source of polio.

In 2017, Andino and his colleagues discovered how OPV reverts to its harmful form: a single mutation restores the virus's capacity to migrate from the human gut and into the nervous system. Within a few years, the group had devised a trio of mutations that make such genetic reversion much less likely and packaged it into a new vaccine.

That vaccine, nOPV2, earned the WHO's first-ever emergency use listing for a vaccine in 2020 and was quickly manufactured and distributed.

"Over 600 million doses were delivered to more than 28 countries, and in ten instances it stopped ongoing outbreaks of vaccine-derived polio," said Andino. "It gave us a lot more confidence that this actually was working as anticipated."

Covering all the bases with polio eradication

Despite its effectiveness, nOPV2 only protects against one of three strains of polio, and cases of polio have recently emerged in Israel, which is heavily vaccinated, as well as in pockets of the US where people refuse to vaccinate their kids.

Even where there are no polio cases in hospitals, polio continues to be detected in wastewater in major cities. There may be 99% fewer polio cases today than there were 30 years ago, but the last 1% has proven hard to snuff out.

"If there's polio anywhere, it will come back where there are gaps in vaccination," Andino said.

The latest work from Andino's group takes the solution they crafted for nOPV2—the three mutations that usually prevent the vaccine from becoming dangerous over time—and engineers it into the other two

types of OPV. The resulting vaccines, nOPV1 and nOPV3, effectively prevented polio in animal models. All three are much safer than the original OPVs, which can occasionally cause paralysis in those who get the vaccine, although this is rare (on the order of one case per two million children vaccinated).

The two new vaccines are currently being tested in clinical trials to ensure that they are both effective and do not revert to dangerous forms in humans. Andino is hopeful they will be incorporated into bivalent or trivalent combinations with nOPV2. Children of the future will be equally protected from polio for life, and perhaps the world will someday experience decades in which zero polio is detected.

"The perception that polio is gone is a dangerous one," said Andino. "For instance, just in India, 500,000 children are born each week, an enormous number of susceptible people. We now have what we need to protect them."

More information: Raul Andino, Developing genetically stable live-attenuated vaccine candidates against type 1 and 3 poliovirus, *Nature* (2023). DOI: 10.1038/s41586-023-06212-3.
www.nature.com/articles/s41586-023-06212-3

Provided by University of California, San Francisco