Advancing polio eradication: A rapid diagnostic test for primary immunodeficiency diseases

PATH

As part of multipronged polio eradication efforts, PATH is supporting the development of a rapid diagnostic screening test that will help in detecting primary immunodeficiency diseases (PIDs), a class of rare genetic disorders that present a challenge for eradication of the poliovirus.

The number of polio cases globally has dropped by more than 99 percent since 1988, but the danger persists that polio will again infect tens of thousands of children annually.[1] The only way to eliminate that danger is to eradicate the disease.

Primary immunodeficiency diseases: A unique risk for poliovirus

An important component in strengthening global polio eradication efforts is effective tools to identify people with PID, who are at a greatly increased risk of continuously shedding the attenuated poliovirus acquired from oral polio vaccine (OPV). Such prolonged viral replication and shedding can result in mutations of the attenuated virus used in OPV into a vaccine-derived poliovirus that is as dangerous as the wild virus it is intended to protect against.

The only methods currently available to identify individuals at risk for PIDs are laboratory based and therefore not adequate for use in the remote areas where OPV administration is the most common. The point-of-care rapid diagnostic test (RDT) PATH is developing will play an important role in identifying people at risk for PID and allowing them to receive appropriate treatment. Testing for PID at the point of care is vitally important to polio surveillance initiatives that are critical to disease eradication and efforts to limit the continued shedding of poliovirus.

OPV has been a key tool in polio eradication initiatives, preventing more than 13 million cases globally.[2] OPV uses a weakened version of the poliovirus that replicates in the intestines for a short period while the body builds immunity. During that period, the weakened vaccine-poliovirus is shed through human waste.

Tools like the rapid diagnostic test for primary immunodeficiency diseases that PATH is advancing are critical to eliminating the danger that poliovirus will re-emerge and infect tens of thousands of children annually. Photo: PATH/Gabe Bienczycki.

In places where sanitation is limited and vaccination rates are low, the vaccine-poliovirus circulates in the community for a short time, due to the shedding, before dying out, sometimes even providing passive immunity to other unvaccinated children while circulating. However, if the circulation continues for a long period of time in an area with low vaccination coverage, in extremely rare cases, the weakened vaccine virus can revert into a dangerous pathogen.

Individuals with PID are less capable of mounting an immune response to clear the OPV-derived infection from their bodies and are therefore capable of shedding the poliovirus for years after vaccination. Overly prolonged viral replication leads to mutated forms of the attenuated poliovirus that potentially result in a dangerous vaccine-poliovirus. Effective point-of-care diagnostics to identify people at risk for PIDs will help facilitate efforts to control ongoing shedding and prevent vaccine-virus transmission, both of which will help reduce the likelihood of emergence of dangerous vaccine-derived poliovirus.

Developing a rapid diagnostic test for primary immunodeficiency diseases

It is therefore important to confirm a diagnosis of this rare genetic disorder before administering OPV. However, current methods for identifying individuals with PID require the use of well-equipped laboratories and trained technicians, which are often far from the remote locations where polio is endemic. The PID RDT that PATH is advancing was intentionally designed for use at the point of care in limited-resource settings and functions by detecting the low immunoglobulin G levels that can provide a surrogate biomarker for PIDs.

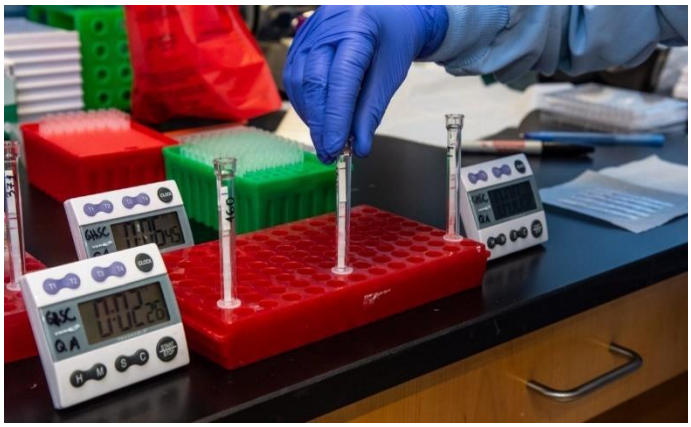
Ensuring this RDT meets the needs and requirements of users has been embedded in all development phases. This has included robust qualitative research with stakeholders and users to guide the development of test specifications.

PATH conducted de novo product development in our in-house research and development laboratory, resulting in early-stage prototypes. The team then made modifications and adaptations to the prototypes based on laboratory assessments of performance against technical requirements. PATH employs rapid prototype iteration to accelerate product development and improve performance. Performance is further supported by full integration of quality assurance activities throughout all phases of development.

PATH advanced three prototype point-of-care PID RDTs to independent expert evaluation in Tunisia in partnership with Institute Pasteur in 2018 and further refined the test based on the evaluation's results and feedback from immunology and polio experts. PATH will conduct additional validation studies on the RDT in 2021 and 2022.

The future of the primary immunodeficiency disease rapid diagnostic test

The evaluation results will determine the path toward commercialization of the PID RDT. PATH has integrated commercial readiness throughout the development process.



PATH has advanced the development of a point-of-care rapid diagnostic test for primary immunodeficiency diseases, including laboratory assessment of prototypes. Photo: PATH/Patrick McKern.

As PID testing advances, there is also a significant opportunity to integrate the test with surveillance systems by turning analog PID RDT results into digital data that could be easily processed and analyzed. This would support better and faster decision-making and the ability to direct appropriate resources where they are most needed.

Learn more

Contact Roger Peck, senior program officer, Diagnostics, at rpeck@path.org for additional information.

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