DIAGNOSTICS

Highly sensitive tests for malaria

Identifying the final cases in areas close to elimination

Detecting low-density infections

Many countries that have implemented successful malaria control programs are now close to achieving the goal of elimination. In these areas, a significant portion of infected individuals have low-density parasite infections with minimal or no symptoms but are still capable of transmitting malaria. However, these low-density infections may not be detected by existing rapid diagnostic tests. The next generation of malaria diagnostic tools must be sensitive enough to detect these infections at the point of care so that they can be treated and the cycle of transmission impeded.

PATH and our partners are advancing the availability of highly sensitive diagnostic tests for malaria to support elimination strategies. PATH takes a portfolio approach, using a rigorous process to identify, advance, commercialize, and scale up the most promising solutions to malaria diagnostic challenges in low-resource, near-elimination settings.

Ten times the sensitivity

The first product in the pipeline of next-generation highly sensitive malaria tests was launched in April 2017. The Alere™ Malaria Ag P.f is an in vitro, qualitative, and ultra-sensitive test developed by Abbott to aid in the diagnosis of *Plasmodium falciparum* malaria infection. It has a greater than ten-fold improvement in detection of the histidine-rich protein 2 (HRP2) antigen of *P. falciparum* malaria in human whole blood over current rapid tests, which will enable better identification of infected individuals with very low parasitemia.[1]

Abbott's Alere™ Malaria Ag P.f is fast, portable, and easy to use, and it can produce immediate sensitive results even in rural and remote areas. This highly sensitive diagnostic may help health care workers to screen asymptomatic cases, enabling the implementation of surveillance and mass screen-and-treat programs that are critical to accelerating malaria elimination. It is a more scalable option as compared to molecular assays that detect parasite genetic material, and it can detect a significant portion of the infectious pool in near-elimination settings. Currently, PATH, the Foundation for Innovative New Diagnostics (FIND), Abbott, and the Bill & Melinda Gates Foundation are supporting studies to demonstrate detection of infection in endemic populations using the Alere™ Malaria Ag P.f test and programmatic impact studies to demonstrate the value of the test in elimination strategies.

Also launched in 2017 was a new enzyme-linked immunosorbent assay (ELISA) laboratory test for *P. falciparum*, the Alere™ Malaria Ag P.f HRP2 ELISA. This ELISA represents a several-fold improvement over other ELISAs without adding complexity or cost to end-user laboratories. The ELISA includes a standardized method and components needed to conduct the test, including appropriate controls, which enables fast and efficient processing of specimens and ensures comparability of results across multiple laboratories and countries. Therefore, this new ELISA can serve as a laboratory confirmation test for reference panel validation and can be used as a reference method for highly sensitive HRP2-based tests for malaria, such as the Alere™ Malaria Ag P.f.

Abbott is handling all ordering, manufacturing, and distribution of the Alere™ Malaria Ag P.f and the Alere™ Malaria Ag P.f HRP2 ELISA. Visit www.alere.com for more information and to order.

The development of the Alere™ Malaria Ag P.f was supported by the Bill & Melinda Gates Foundation. PATH and FIND provided clinical evaluation and technical support. Image: Abbott.

The future of malaria diagnostics

To facilitate the development of new diagnostics for *P. falciparum* malaria, PATH and Precision Antibody collaborated to develop and bring to market custom monoclonal antibodies to HRP2. These antibodies have demonstrated equivalent or better binding properties compared to current commercial antibodies for HRP2 detection, representing a new and robust asset that can be used by rapid diagnostic test manufacturers to develop highly sensitive next-generation tests for malaria.

Currently, PATH is conducting research into biomarkers for *P. falciparum* and *Plasmodium vivax* infections to guide development of new diagnostics. Using clinical samples collected from endemic populations, PATH measured HRP2, lactate dehydrogenase, and parasite nucleic acids throughout the course of malaria infection and applied this information to determine the target performance for new diagnostics for malaria that can best serve the malaria community in its goals to improve patient care and eliminate malaria.

PATH also completed proof of feasibility of early prototypes of tests that address HRP2 and HRP3 deletions, which the Alere™ Malaria Ag P.f cannot detect—potentially paving the way for an even more sensitive test that can identify more asymptomatic cases.

About our work in malaria

PATH works in partnership with national governments, the private sector, and global stakeholders to make a malaria-free world a reality. PATH pursues this goal by expanding the use of lifesaving tools and developing new strategies to create malaria-free communities; working to ensure a steady, affordable, and high-quality supply of drugs and diagnostics; and bringing together public- and private-sector partners to advance the development of malaria vaccines.

PATH/Gabe Biencyzcki

Contact

To learn more about PATH's work in malaria diagnostics, visit http://www.path.org/programs/diagnostics or contact Gonzalo Domingo, scientific director and lead of malaria diagnostics, at dxinfo@path.org.

This project is supported by a grant from the Bill & Melinda Gates Foundation.

Reference

1. Das S, Jang IK, Barney B, et al. Performance of a high-sensitivity rapid diagnostic test for *Plasmodium falciparum* malaria in asymptomatic individuals from Uganda and Myanmar and naive human challenge infections. *American Journal of Tropical Medicine and Hygiene.* 2017;97(5):1540–1550. doi:10.4269/ajtmh.17-0245.

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PATH is a global organization that works to accelerate health equity by bringing together public institutions, businesses, social enterprises, and investors to solve the world's most pressing health challenges. With expertise in science, health, economics, technology, advocacy, and dozens of other specialties, PATH develops and scales solutions—including vaccines, drugs, devices, diagnostics, and innovative approaches to strengthening health systems worldwide.

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Date Published
August 2018