

DIAGNOSTICS

Point-of-care tools for malaria care

Determining glucose-6-phosphate dehydrogenase (G6PD) deficiency to guide patient treatment for *Plasmodium vivax*

The challenge of radical cure

Malaria is an infectious disease caused by the *Plasmodium* parasite that causes disease for millions of people worldwide each year. Malaria is targeted for global elimination—that is, the reduction of transmission until new cases are no longer occurring.

Up to 2.85 billion people may be at risk of infection with *Plasmodium (P.) vivax*, a form of malaria found in Asia, Latin America, and the horn of Africa. *P. vivax* is the most difficult type of malaria to fully treat because a form of the parasite known as the hypnozoite can lie dormant in the liver and cause illness weeks or months after the first infection. *P. vivax* is also hard to eliminate because during these relapses the patient also becomes infective, perpetuating the cycle of infection with *P. vivax* in the community.

All hypnozoites in the body must be killed to completely cure a patient with *P. vivax* and stop the spread of disease. This is known as “radical cure.” Currently, radical cure for *P. vivax* can be achieved only through treatment with 8-aminoquinoline-based drugs such as primaquine and the recently FDA approved drug *Krintafel* (tafenoquine). However, patients deficient in glucose-6-phosphate dehydrogenase (G6PD), an enzyme that helps protect red blood cells from oxidative damage, are at risk of hemolytic anemia when treated with 8-aminoquinolines such as primaquine or tafenoquine.

New G6PD deficiency detection tools are needed

Because of the risk of hemolytic anemia, patients with severe G6PD deficiency should not receive the standard course of primaquine for radical cure of *P. vivax*. Furthermore, because females can carry the gene that causes G6PD deficiency on one or both X chromosomes (known as heterozygosity), these females can have varying levels of G6PD activity, which may put them at risk of adverse reactions to 8-aminoquinolines.

A common hereditary condition known as G6PD deficiency poses a threat to efforts to eliminate *P. vivax* malaria. G6PD testing is essential for patient safety and to accelerate elimination efforts.



Patients with G6PD deficiency are at risk of adverse reactions to radical cure for *P. vivax* malaria, and must be tested at the point of care before being given 8-aminoquinolines. PATH/H. Chivoan

It is estimated that 400 million people worldwide are G6PD-deficient, and the condition is common in areas where malaria is endemic. However, simple and rapid tests for G6PD deficiency are not widely available at the point of care (POC), and the tests that are available are not able to detect heterozygous females with intermediate G6PD activity who may be at risk of hemolytic anemia. A POC diagnostic for G6PD deficiency is needed to enable wide-scale radical cure treatment of patients with *P. vivax* malaria and accelerate elimination of the disease.

Our approach

PATH and our partners are advancing new diagnostic tests for G6PD deficiency that may help guide appropriate clinical care of patients and support *P. vivax* elimination efforts. PATH performed comprehensive analyses of the G6PD diagnostic landscape, conducted prospective comparative studies of G6PD assays, and applied the data to develop target product profiles for tests to support malaria case management. In addition, PATH developed GeoDx, an interactive tool to model demand and cost estimates for various G6PD tests in different geographic and epidemiological settings.

PATH also developed a unique specimen repository containing samples of blood with a range G6PD activity, including deficient and intermediate samples; the repository allows PATH and its partners to draw upon reliable sources of G6PD-deficient

samples to use in the development and evaluation of new diagnostic tests. The specimen repository is available to all manufacturers developing G6PD diagnostic tests to support malaria treatment.

PATH is part of multiple product development partnerships that aim to ensure the availability of G6PD testing options that best meet the needs of healthcare providers managing malaria cases. These new test options are designed to support use of 8-aminoquinolines such as primaquine (the standard treatment for *P. vivax*). We are closely collaborating with GSK to ensure a point-of-care quantitative test for G6PD deficiency is available in malaria-endemic countries to support use of the new single-dose 8-aminoquinoline drug tafenoquine (US brand name *Krintafel*), developed by GSK and Medicines for Malaria Venture. PATH is also looking at use cases beyond malaria programs, as new rapid tests for G6PD may have significant use in newborn screening and other clinical care settings.

A portfolio of G6PD tools

PATH works with multiple diagnostic test developers to develop and evaluate G6PD diagnostic tests with different characteristics to suit the needs of test users. We are advancing quantitative tests that are able to identify all G6PD-deficient patients potentially at risk of clinically significant hemolysis, including heterozygous females with low to intermediate G6PD deficiency. These tests include biosensor devices capable of measuring both a patient's G6PD activity and hemoglobin levels. Qualitative tests with a simple control line readout are also in development, providing a low-cost option for use at the community level to guide administration of primaquine.

These new G6PD diagnostic tests are expected to become available between 2018 and 2020. In addition, PATH has been working with global and in-country partners to increase access to the new POC G6PD diagnostic tests. As new tests come to market, PATH supports and guides manufacturers to facilitate test registration, manufacture, and sale in countries where they are needed most.

Contact

To learn more about G6PD diagnostics, visit <http://www.path.org/programs/diagnostics/> or contact Gonzalo Domingo, scientific director and lead of malaria diagnostics at PATH, at dxinfo@path.org.

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PATH is advancing biosensor devices that provide a reading of G6PD activity and hemoglobin levels. PATH/SD Biosensor

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About PATH's 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 and diagnostics.



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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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