Malaria diagnosis in most endemic countries was largely based on clinical symptoms that are non-specific. This resulted in the over-diagnosis and therefore, over-treatment of malaria, negation of other non-malarial febrile illness, exertion of drug pressures on the malaria parasites with fear of early on-set of drug resistance etc. The gold standard for malaria diagnosis, microscopy, requires high skills, long training, electricity, laboratory equipment, reagents and the turn-around-time for the malaria test could be extremely long in a number of settings and thus not available to guide the prescription of antimalaria medicines. The need for a rapid malaria test was therefore imperative for an effective malaria case management. The availability of good performing malaria rapid diagnostic tests (RDTs) has made the paradigm shift from clinical diagnosis to parasite-based confirmation of malaria a possibility.

In the last decade, millions of RDTs for malaria have been implemented worldwide. These simple and easy-to-use tests can diagnose malaria from blood in about 15 minutes, making a diagnostic possible at all levels of the health system. While the tests have enabled better access to malaria diagnosis, many challenges remain.

Members and panelists from The London School of Hygiene and Tropical Medicine, The Foundation for Innovative New Diagnostics (FIND), The University of Lagos, The University of Yaounde I, PATH, USAID/Deliver Project, and the U.S. Food and Drug Administration (FDA) addressed many challenges in this three-part discussion: interpreting test results in context; the impact of RDTs on the behavior of health care providers; the implications of the WHO “test and treat” guidelines; as well as regulations and procurement issues.

Key Points

- The quality of the RDT procured (in terms of sensitivity, specificity and thermal stability) is critical. There are over 60 companies that manufacture malaria RDTs worldwide with varied performance characteristics. Choosing RDTs should also be dependent on the setting. For example, the prevalent malaria parasite species – Plasmodium falciparum prevalent area will require RDT that targets histidine-rich-protein 2 (HRP-2) while settings with a mixture of both P. falciparum and P. vivax will need a pan-specific RDT or a combination with HRP-2 (combo).
- Quality of RDTs is adversely affected by heat and duration of storage. Some brands are more affected than others. Store tests away from direct sunlight and heat, and perform periodic monitoring of test validity using positive control reagents, such as positive control wells (PCWs) developed by FIND. For example, some tests resist high temperature better than others. (The WHO-FIND RDT Product Testing Programme has demonstrated stability of a number of RDTs during incubation at 45°C or even 60°C. See key references).
- Humidity should not be a problem if the integrity of the RDT pouch is maintained. Before use, RDT pouches should be checked to make sure there is no damage. When performing the test, it must have a positive control line.
- Ensure that tests procured have as long an expiration date as possible. Test kits are more likely to give false negative results close to their expiry date.
- Good transport conditions are critical.
- The manufacturer’s instructions must be strictly followed as the volume of blood, drops of buffer, reading time required differ from product to product. One should ensure that tests procured have as long an expiration date as possible. Test kits are more likely to give false negative results close to their expiry date.
- The accuracy of RDTs is influenced by the proficiency with which RDTs are performed. This is in turn affected by the clarity of instructions included in the test kit, ease of use (how many steps, how complicated are the steps etc) and ease in the interpretation of test results.
- The reading time must be exact, e.g. after the recommended time, false positive test lines can appear.
- The test result can be a faint line if the parasite density of the infection is very low, typically below 100 parasites per microlitre of blood, depending on the product’s quality. However, malaria patients with clinical symptoms have much higher parasite densities, so malaria infections will be detected by RDTs of good quality.
- As RDTs are often performed outside of laboratory settings in many countries, it is important for malaria control programmes to develop quality assurance (QA) systems for RDTs. The development and use of Quality control (QC) panels (e.g PCWs by FIND) can ensure that RDTs are being performed and interpreted correctly.
- A Lab professional in Namibia notes that because tests are easy to perform, many health care providers at district level take quality for granted. “For instance, the volume of blood and the volume of buffer reagent that is used, the time at which the result is read, the presence or absence of a control line which validates the test result itself. Some kits will not come with enough plastic pipettes hence some nurses end up using capillary tubes and estimate the volume or blood sample. I have seen some providers not adhering to these simple but critical steps in conducting the test, which can lead to false results.”
- The end user should be trained and retrained in all aspects of RDTs usage, result interpretation, and treatment initiation.
- Rosana Peeling of the London School of Hygiene & Tropical Medicine notes that malaria control programmes should develop a mechanism to monitor the validity of test kits at temperatures similar to those in field settings so that they can give advance warning to health workers if test kits are failing.
- Community health workers and lay workers must be made aware that there are various non-malaria fever illnesses which were previously treated as malaria. Various studies have demonstrated that the proportion of malaria-related fevers among all fever cases are less than expected, so increased use of parasite-based diagnosis in general must go in parallel with an improved awareness and management of non-malaria fever illnesses.
- Clinicians should be trained in RDTs usage, and be aware of the transmission, seasonality and epidemiology of other malaria-like diseases within their specific regions for differential diagnosis.
- “Involvement of patients may provide an opportunity to improve prescribing practice if their expectations for testing and treatment in line with test results can be effectively communicated to clinicians. A negative test made in the presence of the patient (or caretaker) may make it less tempting to treat for malaria, as is unfortunately still often done. Mismanagement seems higher if the patient is not allowed to see the result.” (Chandler et al. 2008)
Advocacy, Policy, Procurement

- Members noted the value of RDTs for epidemiology and the design of disease control strategies.
- In the 2nd session of the Expert panel, participants debated the WHO “Test and Treat” recommendations for managing malaria and the parasitological confirmation of malaria before treatment initiation. Although the debate is still open (“Studies have shown clear reduction of ACT use with RDTs though cases of fever remains high.”) “However, there is also evidence of no change in prescribing habit following RDT use. In some endemic settings, up to 80% of patients who were parasite negative by RDT still received an antimalarial.”). Training, QA, behavioral change by the health worker and patient education were identified as paramount.

Specific Case

- There is a need to advocate for the use of evidence-based malaria RDTs for clinical decision-making and for the development and implementation of a robust algorithm for clinical differentiation of fevers.
- In the U.S.A, premarket clearance is required in order for malaria RDTs to be distributed nationwide. Malaria RDTs have been classified under 21 CFR 866.3402 as “Plasmodium species antigen detection assays”, Class II devices. A description of these devices can be found in our Code of Federal Regulations. Information on submitting a premarket notification for Malaria RDTs can be found online in the guidance “Class II Special Controls Guidance Document: Plasmodium Species Antigen Detection Assays.” Additional information include a sample FDA review of a cleared assay for Plasmodium species (PDF) and information on marketing a device in the U.S.
- Recognizing the limitations of regulatory authorities in many countries, WHO, FIND, and the CDC have developed a scheme for testing the quality of RDTs (WHO. Malaria rapid diagnostic test performance. Results of WHO product testing of malaria RDTs: round 3. ISBN 978 92 4 150256 6. 2011).
- Lawrence Barat of USAID shared that one of the greatest barriers to implementation in most countries is weak supply chain systems. Even in countries that have successfully scaled-up the use of RDTs at the national level such as Senegal and Ethiopia, stock outs of RDTs at front-line health facilities and at community level are far too common. Short Message Service Solutions for Supply Chain Management has proven to be helpful in other areas.

Key References

- WHO-Regional Office of the Western Pacific/TDR. Evaluation of rapid diagnostic tests: malaria. September 2006 (PDF)
- WHO-FIND-CDC RDT product testing programme
- WHO-FIND Lot testing of Malaria Rapid Diagnostic Tests
- FIND Training materials for malaria RDTs
- FIND Test diagnostique rapide (TDR) du paludisme à P. falciparum: Manuel d'instruction
- FIND Pocket guides on transporting, storing, and handling malaria RDTs
- WHO-WPRO (Western Pacific Regional Office of WHO) Malaria RDTs website
- Chandler et al, The importance of context in malaria diagnosis and treatment decisions - a quantitative analysis of observed clinical encounters in Tanzania, Trop Med Int Health. 2008 (Full text PDF)
- David Bell and Rosanna W. Peeling. Evaluation of rapid diagnostic tests: malaria. Nature Reviews Microbiology, S34-S38 (September 2006) | doi:10.1038/nrmicro1254. WHO–Regional Office for the Western Pacific/TDR (Open access)

Enrich the GHDonline Knowledge Base

Please consider replying to this discussion with the following information

- Share your training material for health workers on RDTs
- Share your strategy for differential diagnosis
- Post your experience with the procurement and financing of RDTs at the program, district, and national level.