Perspective Piece

Factoring Quality Laboratory Diagnosis into the Malaria Control Agenda for Sub-Saharan Africa

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Abstract. Recent progress in malaria control in sub-Saharan Africa has been achieved primarily through provision of insecticide-treated nets, indoor residual spraying, and antimalarial drugs. Although these interventions are important, proper case identification and accurate measurement of their impact depend on quality diagnostic testing. Current availability of diagnostic testing for malaria in sub-Saharan Africa is inadequate to support disease management, prevention programs, and surveillance needs. Challenges faced include a dearth of skilled workforce, inadequate health systems infrastructure, and lack of political will. A coordinated approach to providing pre-service clinical and laboratory training together with systems that support a scale-up of laboratory services could provide means not only for effective malaria case management but also, management of non-malaria febrile illnesses, disease surveillance, and accurate control program evaluation. A synthesis of the challenges faced in ensuring quality malaria testing and how to include this information in the malaria control and elimination agenda are presented.

INTRODUCTION

The call to eliminate malaria in sub-Saharan Africa has been renewed in recent years by the realization that concerted use of interventions, such as insecticide-treated bed nets (ITNs), indoor residual spraying of insecticides (IRS), and prompt case management with effective antimalarials, could make that goal achievable. The international community, realizing the potential, has committed enormous resources through programs such as the US President's Malaria Initiative, Global Fund to Fight AIDS, TB and Malaria, and the Bill and Melinda Gates Foundation. Several African countries now report reductions in malaria disease burden,^{1–4} and although ITN use and IRS are central to these reductions, accurate measurement of their impact to a large extent depends on parasitological confirmation of malaria. The World Health Organization (WHO) currently recommends parasitological confirmation of all suspected malaria cases. However, the current state of malaria laboratory diagnosis in Africa is inadequate to support case management and prevention programs. Malaria diagnosis in Africa is still largely based on clinical signs and symptoms, with the role of laboratories significantly diminished or non-existent.^{5,6} A consequence of the prolonged neglect of laboratories in malaria case management is that, even when quality laboratory services are available, clinicians too frequently ignore negative results.^{7–12}

The reduction in clinical malaria in several countries^{13–16} and the use of expensive artemisinin-based combination therapeutic (ACT) antimalarial drugs call for case management practices that emphasize parasitologic confirmation, because continued use of ACTs in non-malaria cases represents a waste of resources and eventually, is unsustainable. Indiscriminate use of ACTs could create sufficient drug pressure that hastens development of resistant parasites, a situation that has begun to develop in Southeast Asia.^{17–19} Furthermore, identifying febrile cases as having non-malarial causes provides opportunities to treat other potentially debilitating or fatal infections and also avoids unnecessary exposure to adverse events asso-

ciated with ACTs. Therefore, laboratory-confirmed malaria is critical for appropriate management of malaria and other febrile diseases, maintaining the effectiveness of ACTs, and evaluating the effectiveness of interventions. Thus, the importance of parasitologic confirmation needs to be recognized, and its integration into case management and surveillance need to be prioritized and supported with adequate human and financial resources and political will.

EMPHASIZING PRE-SERVICE TRAINING

The recent push for parasitological confirmation of malaria in Africa has highlighted the severe shortage of experienced laboratory technicians and inadequate laboratory infrastructure to meet this need.^{20,21} This finding has led to several attempts at retraining technicians to improve proficiency in malaria diagnosis. Refresher, in-service training of technicians needs to continue where appropriate for short-term needs. However, considering the importance of malaria in Africa, deliberate emphasis on laboratory diagnosis in pre-qualification training for both clinicians and laboratory technicians is needed. Such emphasis could provide the next generation of health workers with a much needed new perspective on the importance of laboratory-confirmed malaria. In addition, this emphasis will ensure the availability of newly trained health workers with more positive attitudes to parasitological diagnosis who require little or no additional training in the short term to boost the number of individuals with malaria laboratory testing expertise. To obtain a critical mass of proficient workers to advance laboratory diagnosis of malaria above current levels, such an effort should be sustained over several years.

SUPPORT FOR RAPID DIAGNOSTIC TEST ROLLOUT AND USE

The lack of good-quality microscopy and the effort needed to develop such capacity means that, in the short term, rapid diagnostic tests (RDTs) will play a significant role in parasitological confirmation of malaria. Minimal training is needed to use RDTs,^{22,23} and assuming good manufacturing quality accompanied by effective quality assurance systems, several

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tests will perform well in the field. The WHO/Foundation for Innovative New Diagnostics (FIND) product performance evaluation²⁴ and pre-procurement lot testing programs ensure that well-performing tests are purchased by recipients of funds from major donors. However, continued vigilance is required in training health workers to perform tests appropriately and eliminating many low-quality RDTs from the market that not only endanger patients who are misdiagnosed but also, have the potential to reverse acceptance of the technology gained by high-quality tests. The introduction of RDTs also argues for revising the traditional roles of non-laboratory health workers, such as nurses and community health workers, to include malaria diagnosis using RDTs. This change is especially relevant in health facilities with no access to laboratory services and qualified technicians.

ADHERENCE TO LABORATORY TEST RESULTS

Malaria case management requires coordinated efforts by several healthcare professionals. For laboratory tests to have a significant impact on malaria control and elimination, a paradigm shift is needed in patient care. The practice of treating patients for malaria when laboratory tests are negative and the risk of severe malaria is low^{8,12} should be discouraged. Professional associations (including those associations for nurses and clinical officers) in endemic countries have a significant role to play in communicating changes in clinical management of malaria to their members. This communication can be done by working with Ministries of Health to develop and communicate concise case management policies and guidelines. Communication on this level has the potential for high positive impact with minimal additional cost. In addition, considering the high malaria prevalence in most African countries, training curricula for health workers can be revised to highlight the need for parasitological diagnosis. However, considering that the WHO recommendation for parasitological diagnosis was issued in 2010, changing existing prescription habits needs to be viewed as a long-term, time-consuming process that requires sustained effort, especially by national malaria control programs and Ministries of Health. Results from a multiyear assessment of the impact of RDT introduction in Senegal²⁵ suggest that this change is possible. In promoting adherence to test results under universal diagnosis, caution is needed to address the limitations of RDTs, particularly with regards to lower sensitivities at low parasite densities and detection of non-falciparum *Plasmodium* species.²⁴

SUBSIDIZED MALARIA CASE MANAGEMENT

In situations that require payment for laboratory tests separately from consultation fees, many febrile patients or their caregivers are known to skip the test and resort to self-medication with easily available antimalarial drugs.²⁶ Provision of free or reduced-cost malaria laboratory testing and ACTs for positive cases needs to be widespread enough within a country to encourage individuals who would otherwise not seek medical care to use health facilities for assessment of symptoms suggestive of malaria and increase the proportion of suspected malaria cases that are parasitologically confirmed. These services could reduce instances where individuals incorrectly self-medicate with antimalarials without appropriate testing or when tests are negative, and they

should be seen as important components of control programs, especially in the early stages of malaria elimination. However, challenges will remain in the inadequately regulated private sector, where financial incentives exist to test and treat patients irrespective of test result.

ACCURATE MALARIA DIAGNOSIS IN CHANGING MALARIA EPIDEMIOLOGY SETTINGS

The changing epidemiology of malaria^{1,13,14,27,28} could result in changes in acquisition of clinical immunity.^{29,30} Possible consequences of reduced immunity could be shifts in age groups in which severe disease occurs, more severe disease in the population, and disease caused by relatively low parasite densities. It is critical that countries have good-quality laboratory capacity to monitor and quickly detect these changes. In routine practice, parasite load is best monitored by good-quality smear microscopy. However, the widespread promotion of RDTs and the longer time required to enhance good-quality malaria microscopy capacity present challenges. Sentinel sites carefully chosen to represent different epidemiological settings within a country with a wide enough representative population can provide valuable information if decent proportions of cases are diagnosed with high-quality microscopy. At the pre-elimination and elimination stages, more sensitive tools, such as polymerase chain reaction (PCR), may be needed to detect and eliminate parasite reservoirs, especially in asymptomatic cases, to interrupt transmission.

INTEGRATED FEVER MANAGEMENT

Eliminating malaria as a cause of fever through testing provides opportunities to examine patients for other potentially life-threatening diseases. When good-quality malaria laboratory diagnosis is available and assuming test results are followed, prescribing of antimalarials to patients with non-malaria fever can be minimized.^{12,31–33} Although resources are currently unavailable to fully equip health centers with a wide array of laboratory tests, periodic systematic evaluation of prevalent non-malarial febrile diseases could be conducted to determine the most critical laboratory tests and suggest what anti-infective agents should be recommended for treatment. Such streamlining would represent a more efficient use of limited resources and could be a portal for integrated clinical and laboratory services for multiple diseases. The availability of medications to treat non-malarial infections will be critical to this integrated approach.

PRIVATE SECTOR HEALTHCARE AND MALARIA DIAGNOSIS

Private, largely unregulated health facilities and laboratories play critical roles in primary healthcare in Africa. Unfortunately, discussions on improving laboratory services often exclude these facilities. Therefore, it is essential that efforts to improve laboratory diagnosis of malaria incorporate private healthcare and other non-governmental facilities. Reference laboratories working within Ministries of Health need to provide clear and concise guidance on diagnostic standards that could include guidance on test selection (e.g., RDTs), standard operating procedures, and job aids. Such standardization will ensure consistent quality of training as well as reduce the

impact of the inevitable health worker mobility within the health system.

Major challenges remain before reaching universal laboratory diagnosis of malaria as recommended by the WHO.³⁴ Overcoming these challenges requires sustained efforts in developing capacity and enhancing the role of the laboratory in malaria case management. The WHO has recently published a manual on universal access to malaria diagnostic testing³⁵ aimed at guiding countries to plan, develop, and maintain malaria diagnostic testing capacity. Malaria control and elimination depend on accurate identification and appropriate treatment of cases. Promoting the laboratory in the effort will make that goal easier to achieve and likely prevent major controversies in estimating disease burden.^{36,37}

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